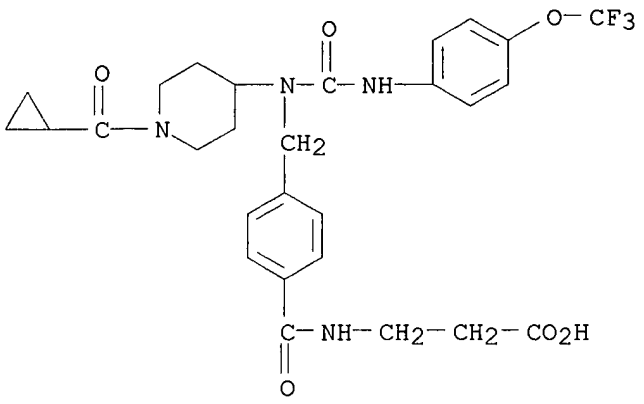


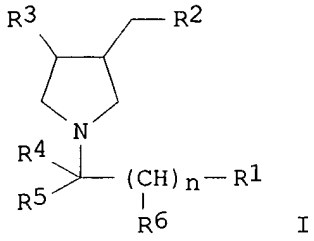
RE.CNT 3
RE
(1) Beecham Group Limited; EP 0000816 A1 1979 HCAPLUS
(2) Mitsui Chemicals Inc; EP 0847992 A1 1998 HCAPLUS
(3) Novo Nordisk AS; WO 9901423 A1 1999 HCAPLUS

L17 ANSWER 8 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:725458 HCAPLUS
DN 133:296372
TI Preparation of 3-phenyl-4-(heterocyclylmethyl)pyrrolidine modulators of chemokine receptor activity
IN Berk, Scott; Caldwell, Charles; Chapman, Kevin; Hale, Jeffrey; Lynch, Christopher; Maccoss, Malcolm; Mills, Sander G.; Willoughby, Christopher
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 200 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

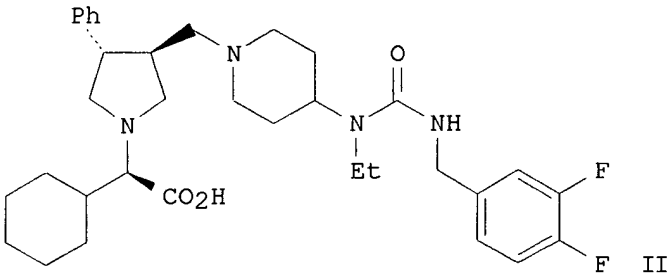
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000059497	A1	20001012	WO 2000-US9059	20000405

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-128174 P 19990406
OS MARPAT 133:296372
GI



I



II

AB The title compds. (I) [wherein R1 = CO2H, NO2, tetrazolyl, hydroxyisoxazole, SO2NH(alkyl)R9, SO2NHCO(alkyl)R9, or PO3H2; R9 = H, (cyclo)alkyl, benzyl, or (un)substituted phenyl; R2 = (un)substituted piperidinyl, tetrahydropyridinyl, or piperazinyl; R3 = (un)substituted Ph or heterocyclyl; R4 = H or (un)substituted alkyl, (alkyl)cycloalkyl, alkenyl, alkynyl, Ph, alkylphenyl, naphthyl, biphenyl, heterocyclyl, cyclohexenyl, etc.; R5 and R6 = independently H or (un)substituted alkyl; or R4 and R5 may be joined together to form an (un)substituted C3-8 cycloalkyl ring; n = 1-3] were prepd. as modulators of chemokine receptors, esp. the chemokine receptors CCR-5 and/or CCR-3. For example, EtNH2 and 1-tert-butoxycarbonyl-4-piperidone were reacted in the presence of DIEA and reduced with NaBH(OAc)3 to give 4-(N-ethylamino)-1-tert-butoxycarbonylpiperidine (97%). Addn. of carbonyldiimidazole and 3,4-difluorobenzylamine to the piperidine followed by deprotection with TFA afforded 4-(N-(N-(3,4-difluorobenzyl)carbamoyl)-N-ethylamino)piperidine.bul.TFA (45%). Coupling the deprotected piperidine with the aldehyde 2-(R)-(3-(R)-formyl-4-(S)-phenylpyrrolidin-1-yl)-2-(cyclohexyl)acetic acid 4-methoxybenzyl ester (prepn. given) in the presence of DIEA followed by redn. with NaBH(OAc)3 gave II. I showed binding activity to the CCR-5 or the CCR-3 receptor, generally with IC50 values of < 1 .mu.M. The present invention is directed to compds. which inhibit the entry of human immunodeficiency virus (HIV) into target cells and are of value in the prevention and treatment of HIV infection and the resulting AIDS syndrome (no data). The invention is further directed to compds. which are useful in the prevention or treatment of certain inflammatory and immunoregulatory disorders, including asthma, allergic rhinitis, dermatitis, conjunctivitis, rheumatoid arthritis, and atherosclerosis (no data).

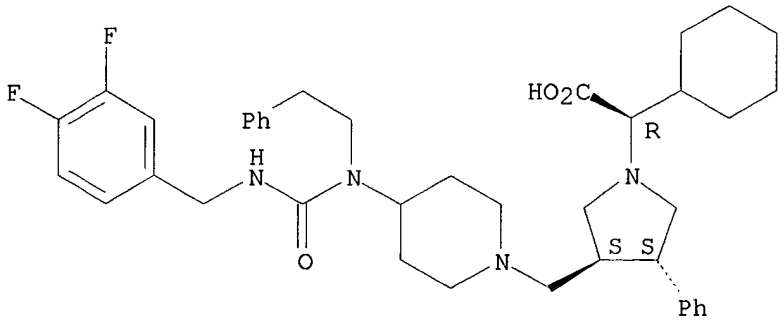
IT **301230-89-7P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of 3-phenyl-4-(heterocyclylmethyl)pyrrolidine chemokine receptor modulators by reaction of 3-phenyl-4-formylpyrrolidines with

heterocycles)
RN 301230-89-7 HCAPLUS
CN 1-Pyrrolidineacetic acid, .alpha.-cyclohexyl-3-[[4-[[[[(3,4-difluorophenyl)methyl]amino]carbonyl](2-phenylethyl)amino]-1-piperidinyl]methyl]-4-phenyl-, (.alpha.R,3S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



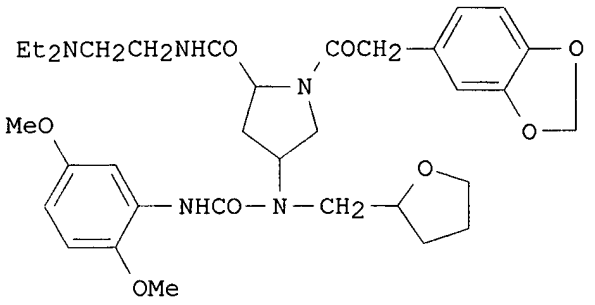
RE.CNT 3
RE
(1) de Laszlo; US 5776954 A 1998 HCAPLUS
(2) Elliott; US 5684032 A 1997
(3) Merck & Co Inc; WO 9909984 A1 1999 HCAPLUS

L17 ANSWER 9 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:645989 HCAPLUS
DN 133:223047
TI Synthesis of proline derivatives
IN Hocker, Michael Douglas; Plunkett, Matthew
PA Axys Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000053579	A2	20000914	WO 2000-US6021	20000308
	WO 2000053579	A3	20001221		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-123631 P 19990310
OS MARPAT 133:223047
GI



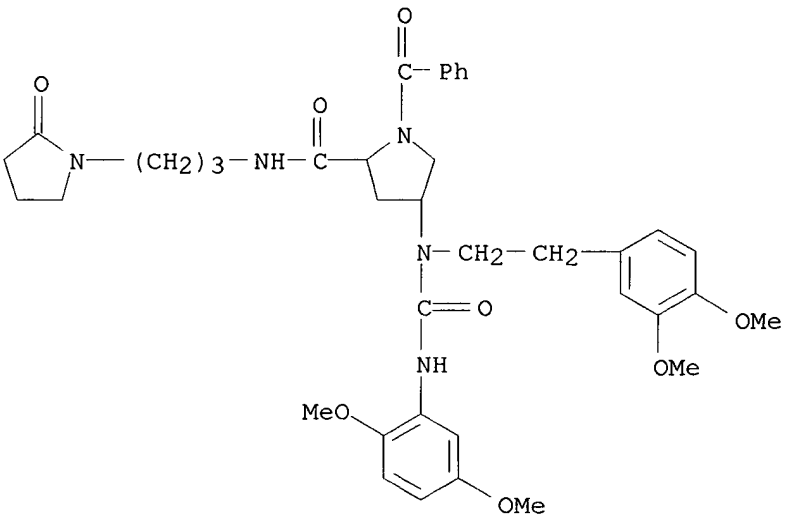
I

AB Compds. R4R5NC(O)-Q-NR1-Y-R2 [R1 is an alkyl radical which may be substituted by tertiary amine, aryl, or heteroaryl; R2 = alkyl, (un)substituted aryl; R4, R5 = cycloalkyl, (un)substituted alkyl or R4R5N is an (un)substituted five to seven membered heterocyclic ring; Q represents a pyrrolidine-2,4-diyl radical which is N-substituted by 2-(un)substituted 2-hydroxyethyl or an acyl group and may be substituted at other ring positions; Y = S, SO, SO2] were prepd. by a process which enables individual, parallel, and simultaneous synthesis of a plurality of compds. Thus, proline deriv. I was prepd. by a protocol involving epoxide ring opening, carboxylic acid acylation, linker activation and amine cleavage.

IT **292177-90-3P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(synthesis of proline derivs.)

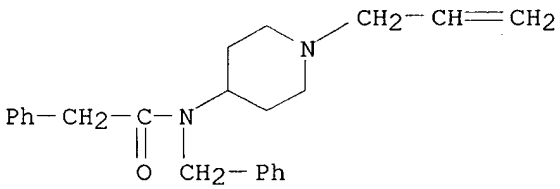
RN 292177-90-3 HCAPLUS

CN 2-Pyrrolidinecarboxamide, 1-benzoyl-4-[[[(2,5-dimethoxyphenyl)amino]carbonyl][2-(3,4-dimethoxyphenyl)ethyl]amino]-N-[3-(2-oxo-1-pyrrolidinyl)propyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 10 OF 29 HCAPLUS COPYRIGHT 2002 ACS

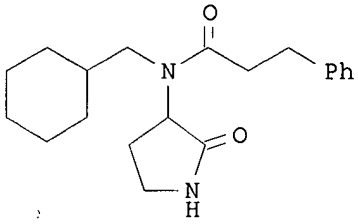
AN 2000:233296 HCAPLUS
DN 133:17050
TI Application of Base Cleavable Safety Catch Linkers to Solid Phase Library Production
AU Wade, Warren S.; Yang, Fan; Sowin, Thomas J.
CS Abbott Laboratories, Abbott Park, IL, 60064-3500, USA
SO Journal of Combinatorial Chemistry (2000), 2(3), 266-275
CODEN: JCCHFF; ISSN: 1520-4766
PB American Chemical Society
DT Journal
LA English
OS CASREACT 133:17050
AB We have used sulfide "Safety Catch" linkers to anchor typical medicinal chem. functional groups to amine resins. Compds. are loaded as the ester, carbamate, or amine. At the end of the synthesis, the linker is activated by peracid. The sulfone resins are then cleaved by .beta.-elimination in the gas phase or in soln. by secondary amines to produce acids and primary, secondary, or tertiary amines. Comparison of cleavage rates to other sulfone resins including SEM showed significantly faster cleavage for this system with conditions similar to Fmoc deprotection. Application of this strategy to a medicinal chem. library gives good yields and purities of the resulting compds.
IT **272777-48-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(application of base cleavable safety catch linkers to solid phase library prodn.)
RN 272777-48-7 HCAPLUS
CN Benzeneacetamide, N-(phenylmethyl)-N-[1-(2-propenyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



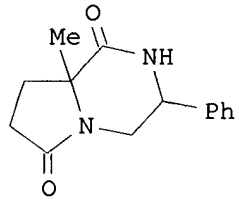
RE.CNT 39
RE
(1) Barlow, K; J Chem Soc, Perkin Trans 2 1977, P1920 HCAPLUS
(2) Bonadies, F; Tetrahedron Lett 1996, V37, P7129 HCAPLUS
(3) Brown, A; J Comb Chem 1999, V1, P283 HCAPLUS
(5) Canne, L; Tetrahedron Lett 1997, V38, P3361 HCAPLUS
(6) Chao, H; J Org Chem 1993, V58, P2640 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:226851 HCAPLUS
DN 133:17439
TI Novel applications of convertible isonitriles for the synthesis of mono and bicyclic .gamma.-lactams via a UDC strategy
AU Hulme, Christopher; Ma, Liang; Cherrier, Marie-Pierre; Romano, Joseph J.; Morton, George; Duquenne, Celine; Salvino, Joseph; Labaudiniere, Richard
CS New Leads Discovery, New Leads Discovery, Rhone-Poulenc Rorer Central

Research, Collegeville, PA, 19426, USA
SO Tetrahedron Letters (2000), 41(12), 1883-1887
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
GI



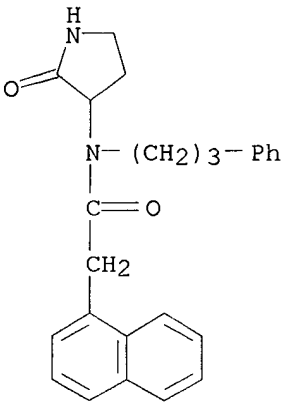
I



II

AB This communication reveals a novel application of the so-called convertible isonitriles for the soln./solid phase generation of .gamma.-lactam analogs. Use of tethered N-BOC aldehydes, e.g., BocNHCH2CH2CHO, in the Ugi multi-component reaction (MCR), followed by BOC removal and base treatment (a "3-step, 1-pot procedure") affords .gamma.-lactams, e.g., I, in good yield. The UDC (Ugi/De-BOC/Cyclize) strategy, coupled with a convertible isonitrile, is now feasible from all three substitution sites of the Ugi product. A conceptually novel approach, combining a bi-functional precursor with a post-condensation modification to give fused lactam-ketopiperazines, e.g., II, is also revealed.

IT **272119-39-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of .gamma.-lactams from carboxylic acids and amines via UDC strategy using isonitriles)
RN 272119-39-8 HCAPLUS
CN 1-Naphthaleneacetamide, N-(2-oxo-3-pyrrolidinyl)-N-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



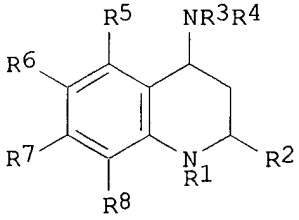
RE.CNT 27

RE
(2) Armstrong, R; Combinatorial Chemistry, Synthesis and Application 1997, P153 HCAPLUS
(3) Baldwin, J; J Chem Soc, Chem Commun 1993, P935 HCAPLUS
(4) Bossio, R; Synthesis 1994, P672 HCAPLUS
(5) Douglas, A; Biochem Soc Trans 1988, V16, P175 HCAPLUS
(6) Flynn, D; J Org Chem 1983, V48, P2424 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 12 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:210122 HCAPLUS
DN 132:236999
TI Preparation of 4-amino-substituted 2-substituted 1,2,3,4-tetrahydroquinolines as CEPT inhibitors
IN Deninno, Michael Paul; Magnus Aryitey, George Tetteh; Ruggeri, Roger Benjamin; Wester, Ronald Thure
PA Pfizer Products Inc., USA
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000017165	A1	20000330	WO 1999-IB1534	19990910
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6140343	A	20001031	US 1999-391313	19990907
	AU 9954403	A1	20000410	AU 1999-54403	19990910
	EP 1114032	A1	20010711	EP 1999-940426	19990910
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9913855	A	20010724	BR 1999-13855	19990910
	NO 2001001349	A	20010514	NO 2001-1349	20010316
PRAI	US 1998-100927	P	19980917		
	WO 1999-IB1534	W	19990910		

OS MARPAT 132:236999
GI



I

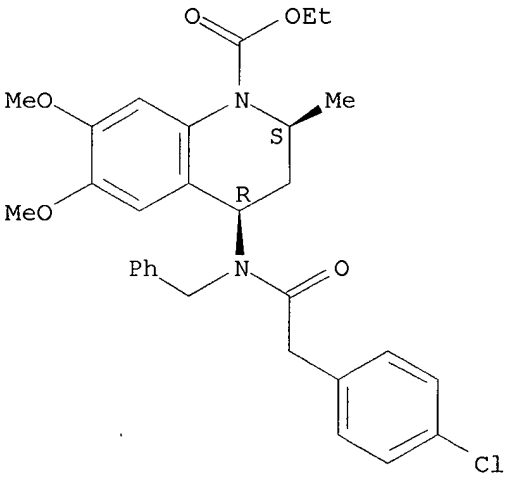
AB The title compds. I [R1 = Y, WX, WY and W = CO, CS, sulfinyl, sulfonyl and X = OY, SY, NHY, NY2 and Y = carbon chain which may be heteroatom replaced; R2 = carbon chain which may be heteroatom replaced; R3 = H, Q and Q = carbon chain which may be heteroatom replaced; R4 = cyano, CHO, etc.; R5-R8 = H, bond, nitro, halo], cholesteryl ester transfer protein inhibitors, were prepd. E.g., Et cis-4-(benzylformylamino)-6,7-dimethoxy-2-methyl-3,4-dihydro-2H-quinoline-1-carboxylate was prepd.

IT **261946-61-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino-substituted tetrahydroquinolines as CEPT inhibitors)

RN 261946-61-6 HCAPLUS

CN 1(2H)-Quinolinecarboxylic acid, 4-[[(4-chlorophenyl)acetyl](phenylmethyl)amino]-3,4-dihydro-6,7-dimethoxy-2-methyl-, ethyl ester, (2R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 1
RE
(1) Bayer Ag; EP 0818448 A 1998 HCAPLUS

L17 ANSWER 13 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1999:495272 HCAPLUS
DN 131:130011
TI Preparation of N-acyl-2-aminoacetamides and cyclization products thereof.
IN Hulme, Christopher; Morton, George C.; Salvino, Joseph M.; Labaudiniere, Richard F.; Mason, Helen J.; Morrissette, Matthew M.; Ma, Liang; Cherrier, Marie-Pierre
PA Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SO PCT Int. Appl., 156 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9938844	A1	19990805	WO 1999-US1923	19990129
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9924821	A1	19990816	AU 1999-24821	19990129
	EP 1051397	A1	20001115	EP 1999-904421	19990129
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
	BR 9908207	A	20001128	BR 1999-8207	19990129
	NO 2000003792	A	20000927	NO 2000-3792	20000724
PRAI	US 1998-73007	A2	19980129		
	US 1998-98404	A2	19980831		
	US 1998-98708	A2	19980901		
	US 1998-101056	A2	19980918		
	WO 1999-US1923	W	19990129		

OS MARPAT 131:130011

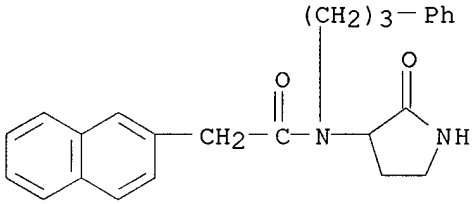
AB RaRbNCRcaRcbRd Ra = RaaCO; Dd = CONHRda; Raa, Rb, Rca, Rcb = H, (substituted) aliphatyl, aryl; Rda = (substituted) aliphatyl, aryl; with provisos were prepd. by reaction of RcaCORcb with RbNH2, RaCO2H, and NCRda. Title compds. may be prepd. on a isocyanide resin and deprotected/cyclized to give 1,4-benzodiazepine-2,5-diones, diketopiperazines, ketopiperazines, lactams, 1,4-benzodiazapines, and dihydroquinoxalinones.

IT **234781-50-1P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-acyl-2-aminoacetamides and cyclization products thereof)

RN 234781-50-1 HCAPLUS

CN 2-Naphthaleneacetamide, N-(2-oxo-3-pyrrolidinyl)-N-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



RE.CNT 3

RE

(1) Boehm; Journal of Organic Chemistry 1986, V51, P2307 HCAPLUS

(2) Failli; Canadian Journal of Chemistry 1973, V51, P2769 HCAPLUS

(3) Fukuyama; Tetrahedron Letters 1981, V22(42), P4155 HCAPLUS

L17 ANSWER 14 OF 29 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:227936 HCAPLUS

DN 130:282070

TI Preparation of N-[[1-(4-cyanobenzyl)-1H-imidazol-5-yl]methyl]piperidines and analogs as farnesyl protein transferase inhibitors

IN Anthony, Neville J.; Gomez, Robert P.; Wai, John S.; Embrey, Mark W.; Fisher, Thorsten E.
PA Merck and Co., Inc., USA
SO U.S., 91 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5891889	A	19990406	US 1997-831308	19970401
	US 6248756	B1	20010619	US 1999-248883	19990211
PRAI	US 1996-14791	P	19960403		
	US 1997-831308	A3	19970401		

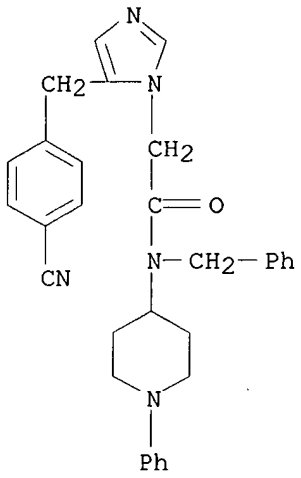
OS MARPAT 130:282070
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention is directed to compds. which inhibit farnesyl-protein transferase (FPTase) and the farnesylation of the oncogene protein Ras. The invention is further directed to chemotherapeutic compns. contg. the compds., and methods for inhibiting FPTase and Ras farnesylation using them. In particular, title compds. I and II and their pharmaceutically acceptable salts are claimed [wherein Ar = (un)substituted Ph; R1 = H, Me; Q1 = (un)substituted (CH2)0-4; X = bond, CH2, CO, (un)substituted NHCO, S, SO, or SO2; Y = H, (un)substituted alkyl, OH or derivs., SH or derivs., NH2 or derivs., etc.; X1 = bond, (un)substituted NHCO or NH, O, S, SO, SO2; A1,A2 = bond, CH:CH, CO, O, (alkyl)imino, etc.; Q2 = (un)substituted (CH2)0-2; Z = (un)substituted aryl; addnl. substituents allowed on piperidine ring]. Over 130 invention compds. and numerous intermediates were prepd. For instance, the invention compd. III was claimed in particular, and was prepd. in 5 steps. Thus, Et isonipecotate underwent a sequence of: (1) N-protection with BOC; (2) deprotonation and alkylation in the 4-position using NaN(SiMe3)2 and 3-(CF3O)C6H4CH2Br; (3) redn. of the Et ester to a hydroxymethyl group using LiAlH4; (4) removal of the BOC group with HCl; and (5) reductive alkylation at N using 1-(4-cyanobenzyl)imidazole-5-carboxaldehyde and NaBH3CN, yielding III after chromatog. In a test for inhibition of farnesylation of Ras-CVIM with human FPTase in vitro, almost all example compds. had IC50 of .ltoreq. 50 .mu.M.

IT **198648-44-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of [[(cyanobenzyl)imidazolyl]methyl]piperidines and analogs as farnesyl protein transferase inhibitors)

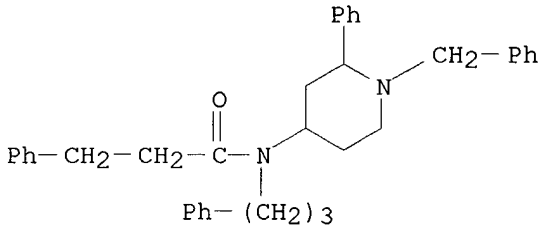
RN 198648-44-1 HCAPLUS
CN 1H-Imidazole-1-acetamide, 5-[(4-cyanophenyl)methyl]-N-(phenylmethyl)-N-(1-phenyl-4-piperidinyl)-, hydrochloride (5:6) (9CI) (CA INDEX NAME)



●6/5 HCl

RE.CNT 21
RE
(1) Anon; EP 0313984 A1 1989 HCAPLUS
(2) Anon; WO 9630343 1996 HCAPLUS
(3) Anon; WO 9631501 1996 HCAPLUS
(4) Anon; WO 9637204 1996 HCAPLUS
(5) Anon; WO 9718813 1997 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

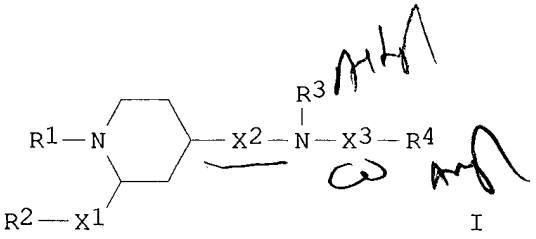
L17 ANSWER 15 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1998:233891 HCAPLUS
DN 128:308380
TI Combinatorial synthesis of dihydropyridone libraries and their derivatives
AU Creswell, Mark W.; Bolton, Gary L.; Hodges, John C.; Meppen, Malte
CS Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SO Tetrahedron (1998), 54(16), 3983-3998
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science Ltd.
DT Journal
LA English
AB Polymer-supported quench methodol. has been used for parallel purifn. of combinatorial libraries of dihydropyridones and their derivs. The dihydropyridone scaffold was assembled via a soln.-phase, Lewis-acid-catalyzed hetero-Diels-Alder reaction. Further modifications allow for the rapid generation of subsequent aminopiperidine and (acylamino)piperidine libraries utilizing a library-from-library approach.
IT **206432-85-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(combinatorial synthesis of dihydropyridone libraries and their derivs.)
RN 206432-85-1 HCAPLUS
CN Benzenepropanamide, N-[2-phenyl-1-(phenylmethyl)-4-piperidinyl]-N-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 16 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:803811 HCAPLUS
DN 128:93188
TI Preparation and formulation of substituted piperidineamines as p antagonists for treating social phobia
IN Struck, Michael; Vassout, Annick; Katz, Richard; Bennett, Deborah; Kramer, Lynn; Hauser, Kathleen
PA Novartis A.-G., Switz.; Struck, Michael; Vassout, Annick; Katz, Richard; Bennett, Deborah; Kramer, Lynn; Hauser, Kathleen
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9745119	A1	19971204	WO 1997-EP2481	19970515
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9728982	A1	19980105	AU 1997-28982	19970515
PRAI	US 1996-18336		19960524		
	WO 1997-EP2481		19970515		

OS MARPAT 128:93188
GI



I

AB The invention relates to the use of substituted piperidineamines I or of a pharmaceutically utilizable salt thereof, in which R1 is an unsubstituted or substituted aralkyl, aryloxyalkyl, heteroaralkyl, aroyl, heteroaroyl,

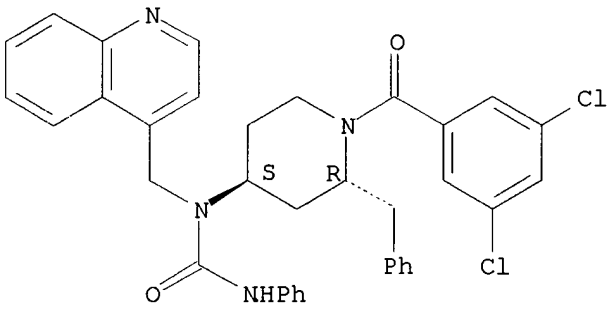
cycloalkylcarbonyl, aralkanoyl, heteroarylalkanoyl, aralkoxycarbonyl or arylcarbamoyl radical or the acyl radical of an .alpha.-amino acid which is unsubstituted or N-substituted by lower alkanoyl or carbamoyl-lower-alkanoyl; R2 is cycloalkyl or an unsubstituted or substituted aryl or heteroaryl radical; R3 is hydrogen, alkyl, carbamoyl or an alkanoyl or alkenoyl radical which is unsubstituted or substituted by carboxyl or esterified or amidated carboxyl; R4 is an unsubstituted or substituted aryl or unhydrogenated or partially hydrogenated heteroaryl radical; X1 is methylene, ethylene, a direct linkage, a carbonyl group which may be ketalized, or an unetherified or etherified hydroxymethylene group; X2 is alkylene, carbonyl or a direct linkage; and X3 is carbonyl, oxo-lower-alkylene, oxo(aza)-lower-alkylene or an alkylene radical which is unsubstituted or substituted by Ph, hydroxymethyl, carboxyl which may be esterified or amidated, or by hydroxyl in a position higher than .alpha.; for producing pharmaceutical products for the treatment of social phobia. Thus, the prepn. and formulation of (2R,2S)-2-benzyl-1-(2-naphthoyl)-N-(4-quinolylmethyl)-4-piperidineamine as p antagonists for treating social phobia, are reported.

IT **150707-99-6P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and formulation of substituted piperidineamines as p antagonists for treating social phobia)

RN 150707-99-6 HCAPLUS

CN 4-Piperidinamine, 1-(3,5-dichlorobenzoyl)-N-[(phenylamino)carbonyl]-2-(phenylmethyl)-N-(4-quinolinylmethyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L17 ANSWER 17 OF 29 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:696746 HCAPLUS

DN 128:3708

TI N-(Amidinophenyl)-N'-substituted-3H-2,4-diazepin-3-one derivatives as factor Xa inhibitors

IN Maduskuie, Thomas Peter, Jr.; Galemmo, Robert Anthony, Jr.; Dominguez, Celia; Quan, Mimi Lifen; Rossi, Karen Anita; Stouten, Petrus Fredericus Wilhelmus; Sun, Jung Hui; Wells, Brian Lloyd

PA Du Pont Merck Pharmaceutical Company, USA

SO PCT Int. Appl., 183 pp.
CODEN: PIXXD2

DT Patent

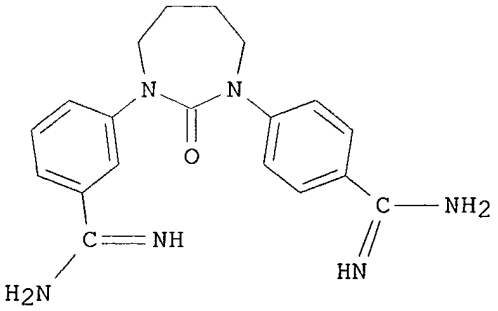
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9738984	A1	19971023	WO 1997-US6431	19970417
	W: AM, AU, AZ, BR, BY, CA, CN, CZ, EE, HU, IL, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5925635	A	19990720	US 1997-838246	19970416
	CA 2251394	AA	19971023	CA 1997-2251394	19970417
	AU 9727339	A1	19971107	AU 1997-27339	19970417
	EP 960104	A1	19991201	EP 1997-921242	19970417
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
PRAI	US 1996-15684		19960417		
	US 1996-647127		19960509		
	US 1997-42532		19970401		
	US 1997-838246		19970416		
	WO 1997-US6431		19970417		

OS MARPAT 128:3708

GI



I

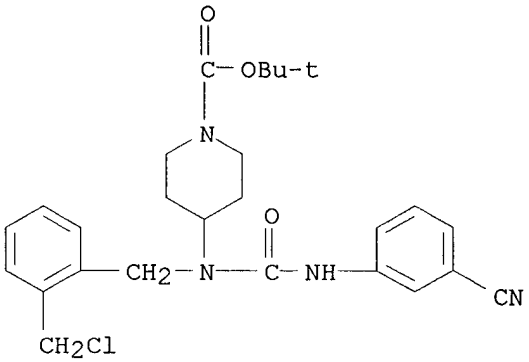
AB Title compds. and some related compds. were prepd. for use as anticoagulants (no data). Thus, 3-NCC6H4NH2 was treated with 4-NCC6H4NCO to give the urea which was cyclized with Br(CH2)4Br and subjected to aminolysis to give the diazepinone I.

IT **198823-73-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of N-(amidinophenyl)-N'-substituted-3H-2,4-diazepin-3-one derivs. as factor Xa inhibitors)

RN 198823-73-3 HCAPLUS

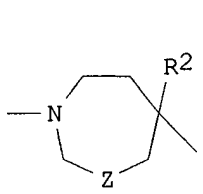
CN 1-Piperidinecarboxylic acid, 4-[[[2-(chloromethyl)phenyl]methyl][[(3-cyanophenyl)amino]carbonyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



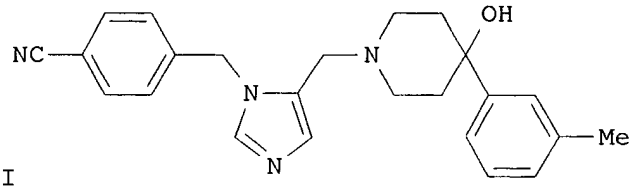
L17 ANSWER 18 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1997:696612 HCAPLUS
DN 127:358860
TI Preparation of 1-(4-cyanobenzyl)-5-piperidinomethylimidazoles as farnesyl protein transferase inhibitors
IN Anthony, Neville J.; Dinsmore, Christopher; Gomez, Robert P.; Hutchinson, John H.; Wai, John S.; Williams, Theresa M.; Bell, Ian M.; Embrey, Mark W.; Fisher, Thorsten E.
PA Merck & Co., Inc., USA; Anthony, Neville J.; Dinsmore, Christopher; Gomez, Robert P.; Hutchinson, John H.; Wai, John S.; Williams, Theresa M.; Bell, Ian M.; Embrey, Mark W.; Fisher, Thorsten E.
SO PCT Int. Appl., 326 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9738665	A2	19971023	WO 1997-US6487	19970327
	WO 9738665	A3	19971127		
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2249601	AA	19971023	CA 1997-2249601	19970327
	AU 9727347	A1	19971107	AU 1997-27347	19970327
	AU 715202	B2	20000120		
	EP 944388	A2	19990929	EP 1997-921256	19970327
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 2001519766	T2	20011023	JP 1997-537388	19970327
PRAI	US 1996-14791	P	19960403		
	GB 1996-9981	A	19960513		
	WO 1997-US6487	W	19970327		

OS MARPAT 127:358860
GI



I



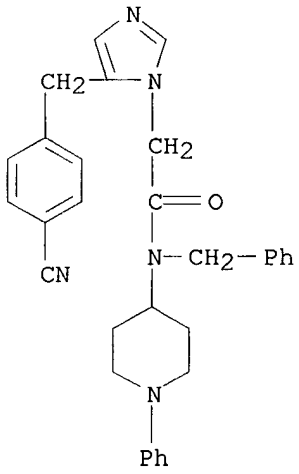
II

AB RA1[C(R1a)2]nA2[C(R1a)2]nZ1[C(R1b)2]pXZ2X1[C(R1c)2]vR1 [I; A1,A2 = bond, CH:CH, CO, O, (alkyl)imino, etc.; R = H, (un)substituted heterocyclyl, -aryl, etc.; R1 = (un)substituted heterocyclyl or -aryl; R1a,R1b = H, OH, alkyl, alkoxy, aryl, etc.; R1c = H, alkyl, aryl, etc.; X = bond, CH2, CO, etc.; X1 = bond, CH2, CO, O, etc.; Z1 = (un)substituted heterocyclylene; Z2 = azacycloalkylene group I; R2 = H, hydroxy(alkyl), alkoxy(alkyl), alkyl, etc.; Z = bond or CH2; p,n = 0-4; v = 0-2] were prepd. Thus, 1-(4-cyanobenzyl)-5-imidazolecarboxaldehyde was reductively aminated by 4-(3-methylphenyl)-4-hydroxypiperidine (prepn. each given) to give title compd. II. Data for biol. activity of I were given.

IT **198648-44-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-(4-cyanobenzyl)-5-piperidinomethylimidazoles as farnesyl protein transferase inhibitors)

RN 198648-44-1 HCAPLUS

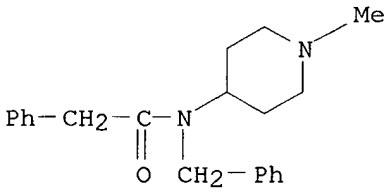
CN 1H-Imidazole-1-acetamide, 5-[(4-cyanophenyl)methyl]-N-(phenylmethyl)-N-(1-phenyl-4-piperidinyl)-, hydrochloride (5:6) (9CI) (CA INDEX NAME)



●6/5 HCl

L17 ANSWER 19 OF 29 HCAPLUS COPYRIGHT 2002 ACS

AN 1997:484079 HCAPLUS
DN 127:205518
TI Rapid in-plate generation of benzimidazole libraries and amide formation using EEDQ
AU Thomas, James B.; Fall, Michael J.; Cooper, Julie B.; Burgess, Jason P.; Carroll, F. Ivy
CS Chem. and Life Sciences, Research Triangle Inst., Research Trianlge Park, NC, 27709, USA
SO Tetrahedron Lett. (1997), 38(29), 5099-5102
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
OS CASREACT 127:205518
AB A soln. phase method for the prepn. of etonitazene-related benzimidazoles and a general method for the prepn. of amide derivs. in 96-well format have been developed for the generation of libraries of compds. in parallel.
IT **194538-00-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of etonitazene-related benzimidazoles and amide derivs.)
RN 194538-00-6 HCAPLUS
CN Benzeneacetamide, N-(1-methyl-4-piperidinyl)-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



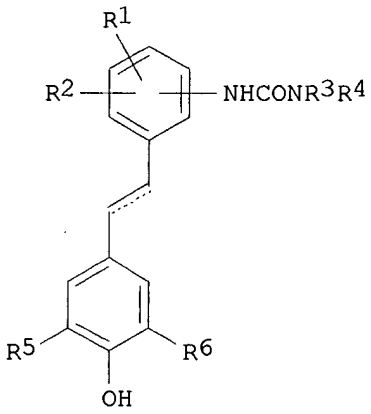
L17 ANSWER 20 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1995:305316 HCAPLUS
DN 122:80893
TI Preparation of substituted aryl ureas as ACAT inhibitors.
IN Sueda, Noriyoshi; Yamada, Kazuhiko; Yanai, Makoto; Miura, Katsutoshi; Horigome, Masato; Oshida, Norio; Hiramoto, Shigeru; Katsuyama, Koichi; Nakata, Fumihisa; et al.
PA Nisshin Flour Milling Co., Ltd., Japan
SO Eur. Pat. Appl., 119 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 625507	A2	19941123	EP 1994-303568	19940519
	EP 625507	A3	19941130		
	EP 625507	B1	19970723		
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
	CA 2123728	AA	19941122	CA 1994-2123728	19940517
	US 5621010	A	19970415	US 1994-245013	19940518

	JP 07258200	A2	19951009	JP 1994-129838	19940520
PRAI	JP 1993-119786		19930521		
	JP 1993-285525		19931021		
	JP 1994-32040		19940204		

OS MARPAT 122:80893

GI



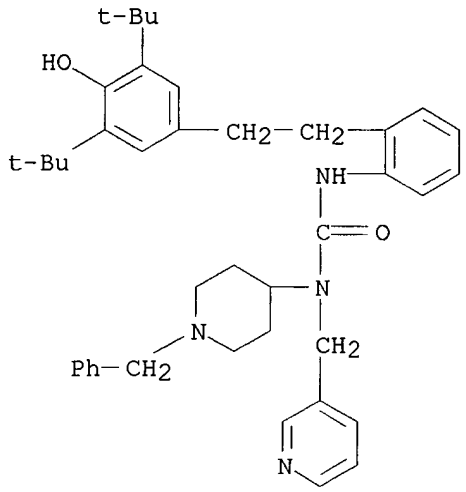
I

AB Title compds. I (R1, R2 = H, halo, C1-6 alkyl, C1-6 alkoxy; R3, R4 = H, C1-12 alkyl, C2-20 alkenyl, substituted amino, hydroxy-, oxoalkyl, bi-, tricycloalkyl, , aryl, heterocyclyl, etc.;R5, R6 = C1-6 alkyl, CH2CH2, CH:CH) or a salt thereof, useful as ACAT (acyl CoA cholesterol acyltransferase) inhibitors, antioxidative activity and lowering blood cholesterol, are prepd. ACAT, antioxidative and cholesterol-lowering activities by I was demonstrated. Diphenylphosphorylazide, 4-(hexyloxy)benzoic acid, Et3N and 4-(2-aminophenethyl)-2,6-di-tert-butylphenol were reacted to give I (R1 = R2 = R3 = H, R4 = 4-(n-C6H13)C6H4, R5 = R6 = Me3C). Pharmaceutical formulations comprising I are given.

IT **160356-63-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted aryl ureas as ACAT inhibitors)

RN 160356-63-8 HCAPLUS

CN Urea, N'-[2-[2-[3,5-bis(1,1-dimethylethyl)-4-hydroxyphenyl]ethyl]phenyl]-N-[1-(phenylmethyl)-4-piperidinyl]-N-(3-pyridinylmethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 21 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:700759 HCAPLUS
DN 121:300759
TI Substituted carbamoyl and oxycarbonyl derivatives of biphenylmethylamines
IN Ashton, Wallace T.; Chang, Linda L.; Greenlee, William J.; Hutchins, Steven M.; Rivero, Ralph A.
PA Merck and Co., Inc., USA
SO Brit. UK Pat. Appl., 122 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

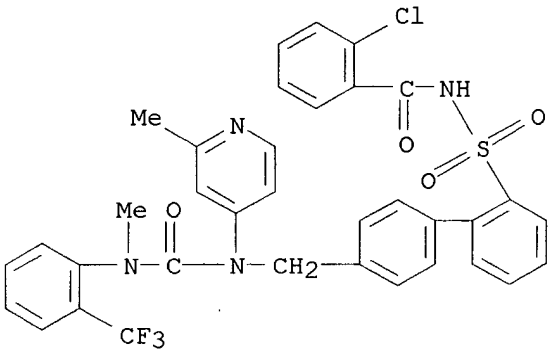
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2268743	A1	19940119	GB 1993-14787	19930716
	US 5312820	A	19940517	US 1992-917642	19920717
PRAI	US 1992-917642		19920717		

OS MARPAT 121:300759
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Carbamoyl and oxycarbonyl derivs. of biphenylmethylamines I (R1 = carboxy, carbamoyl, sulfonyl, etc.; R2, R3 = H, halo, alkyl, etc.; R6 = alkyl, etc.; R8 H, halo, alkyl, etc.; A, B, C, D = CH: or N:; X = O, V = H, alkoxy, etc.) were disclosed as angiotensin-II antagonists with balanced AT1 and AT2 activity useful in the treatment of hypertension and related disorders and ocular hypertension. Specifically claimed example compds. are 1-[N-[[2'-[(2-chlorobenzoyl)sulfamoyl]biphenyl-4-yl]methyl]-N-pentylcarbamoyl]indoline (II) or 1-[[2'-[N-(3-chloro-2-furoyl)sulfamoyl]biphenyl-4-yl]methyl]-3-methyl-1-pentyl-3-[2-(trifluoromethyl)phenyl]urea (III). The possible uses of I as antidepressants (no data) and for the treatment of schizophrenia (no data) were mentioned.

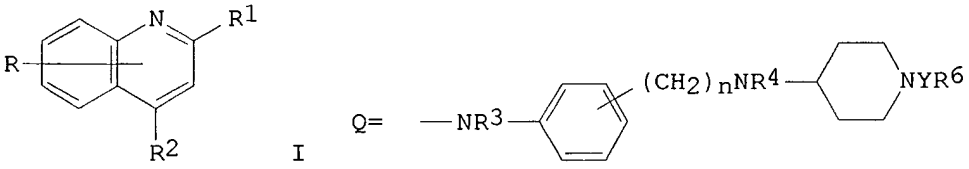
IT **159005-38-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 159005-38-6 HCAPLUS
CN Benzamide, 2-chloro-N-[[4'-[[(2-methyl-4-pyridinyl)[[methyl[2-(trifluoromethyl)phenyl]amino]carbonyl]amino]methyl][1,1'-biphenyl]-2-yl]sulfonyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 22 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1994:106792 HCAPLUS
DN 120:106792
TI N-substituted aminoquinoline analgesic agents
IN Mobilio, Dominick; Musser, John H.
PA American Home Products Corp., USA
SO U.S., 13 pp. Cont. -in-part of U.S. Ser. No. 592,411, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5216165	A	19930601	US 1992-855397	19920320
PRAI US 1990-592411		19901003		

OS MARPAT 120:106792
GI



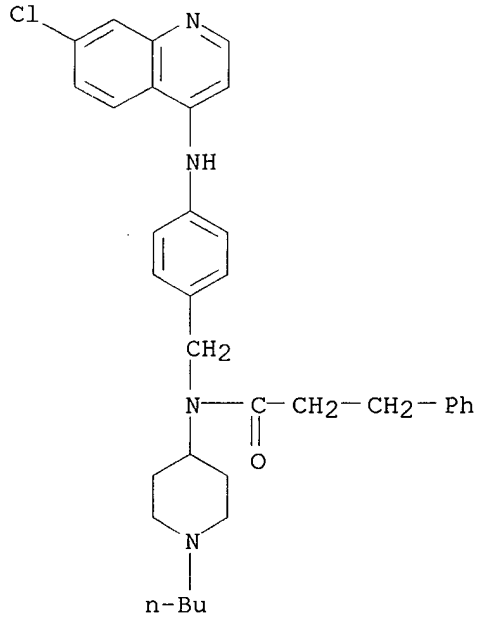
AB The title compds. I [R = H, halogen, CF3; R1, R2 = H, Q; R3 = H, alkyl; R4 = H, COR5; R5 = H, (un)substituted alkyl, Ph; R6 = alkyl, cycloalkyl, arylalkyl, etc.; Y = CO, direct bond; such that when R1 = H then R2 = Q, and when R2 = H then R1 = Q], which antagonize bradykinin and are useful as analgesic agents in the treatment and management of pain, are prepd.

Thus, N-[4-[[(1-butyl-4-piperidinyl)amino]methyl]phenyl]-7-chloro-4-quinolinamine was reacted with hydrocinnamoyl chloride and treated with methanolic HCl, producing N-(1-butyl-4-piperidinyl)-N-[[4-[(7-chloro-4-quinolinyl)amino]phenyl]methyl]benzenepropanamide hydrochloride (II). II had 50% bradykinin inhibitory concn. with guinea pig ileum, of 1.6 .mu.M.

IT **150514-43-5**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(analgesic activity of)

RN 150514-43-5 HCAPLUS

CN Benzenepropanamide, N-(1-butyl-4-piperidinyl)-N-[[4-[(7-chloro-4-quinolinyl)amino]phenyl]methyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 23 OF 29 HCAPLUS COPYRIGHT 2002 ACS

AN 1993:671005 HCAPLUS

DN 119:271005

TI Preparation of 1-acylpiperidine derivatives and their use as substance P antagonists

IN Schilling, Walter; Ofner, Silvio; Veenstra, Siem J.

PA Ciba-Geigy A.-G., Switz.

SO Eur. Pat. Appl., 108 pp.
CODEN: EPXXDW

DT Patent

LA German

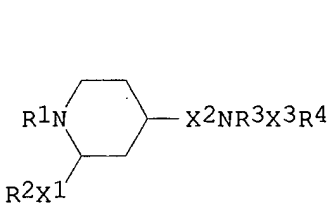
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 532456	A1	19930317	EP 1992-810594	19920804
EP 532456	B1	19950329		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 120456	E	19950415	AT 1992-810594	19920804

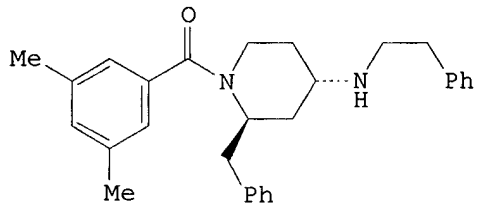
	ES 2070617	T3	19950601	ES 1992-810594	19920804
	CA 2075684	AA	19930213	CA 1992-2075684	19920810
	AU 9220965	A1	19930304	AU 1992-20965	19920810
	AU 660180	B2	19950615		
	IL 102769	A1	19990126	IL 1992-102769	19920810
	NO 9203123	A	19930215	NO 1992-3123	19920811
	ZA 9206013	A	19930331	ZA 1992-6013	19920811
	US 5310743	A	19940510	US 1992-929186	19920811
	HU 67088	A2	19950130	HU 1992-2615	19920811
	JP 07196649	A2	19950801	JP 1992-214093	19920811
	JP 3118090	B2	20001218		
	RU 2114829	C1	19980710	RU 1992-5052784	19920811
	CN 1089261	A	19940713	CN 1993-100018	19930103
	CN 1042335	B	19990303		
	US 5541195	A	19960730	US 1994-196360	19940404
	US 5646144	A	19970708	US 1995-482704	19950607
	FI 9604117	A	19961014	FI 1996-4117	19961014
	NO 9703117	A	19930215	NO 1997-3117	19970704
PRAI	CH 1991-2374	A	19910812		
	FI 1992-3575	A	19920810		
	US 1992-929186	A3	19920811		
	US 1994-196360	A3	19940404		

OS MARPAT 119:271005

GI



I



II

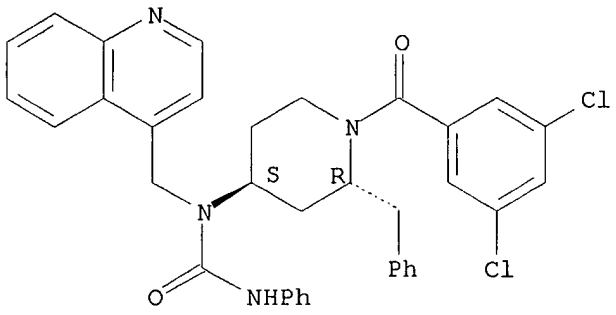
AB Title compds. [I; R1 = (substituted) aralkyl, aryloxyalkyl, aroyl, arylcarbamoyl, heteroaroyl, cycloalkylcarbonyl, aralkanoyl, aralkoxycarbonyl, .alpha.-araminoacid ocyl residue, etc.; R2 = cycloalkyl, (substituted) (hetero)aryl; R3 = H, alkyl carbamoyl, (substituted) alkanoyl, alkenoyl; (R4 = (substituted) aryl, (partially hydrogenated) heteroaryl; X1 = (H2, CH2CH2, bond, (ketalized) CO, (etherified) HOCH; X2 = alklylene, CO, bond; X3 = CO, oxoalkylene, oxoazaalkylene, hydroxyalkylene, etc.], were prepd. Thus, Et (R)-3-amino-4-phenylbutyrate was converted to (2R, 4RS)-2-benzyl-1-(3,5-dimethylbenzoyl)-4-piperidineamine in several steps and the latter was stirred with PhCH2CHO, NaOAc, HOAc, and NaBH3CN in MeOH to give title compd. II and its diastereomer. I inhibited substance P-induced blood vessel dilation in guinea pig ears beginning at 0.01 mg/kg i.v.

IT **150707-99-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as substance P antagonist)

RN 150707-99-6 HCAPLUS

CN 4-Piperidinamine, 1-(3,5-dichlorobenzoyl)-N-[(phenylamino)carbonyl]-2-(phenylmethyl)-N-(4-quinolinylmethyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L17 ANSWER 24 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1986:68856 HCAPLUS
DN 104:68856
TI Bicyclic heterocyclyl containing N-(bicyclic heterocyclyl)-4-piperidinamines
IN Janssens, Frans Eduard; Torremans, Joseph Leo Ghislanus; Hens, Jozef Francis; Van Offenwert, Theophilus Theresia J. M.
PA Janssen Pharmaceutica N. V., Belg.
SO Eur. Pat. Appl., 106 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 144101	A2	19850612	EP 1984-201611	19841107
EP 144101	A3	19850724		
EP 144101	B1	19910206		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
US 4695569	A	19870922	US 1984-660608	19841012
AT 60769	E	19910215	AT 1984-201611	19841107
SU 1500162	A3	19890807	SU 1984-3814401	19841123
CA 1257258	A1	19890711	CA 1984-468587	19841126
CZ 281114	B6	19960612	CZ 1984-9128	19841128
SK 278443	B6	19970507	SK 1984-9128	19841128
DK 8405678	A	19850531	DK 1984-5678	19841129
FI 8404708	A	19850531	FI 1984-4708	19841129
FI 80446	B	19900228		
FI 80446	C	19900611		
NO 8404755	A	19850531	NO 1984-4755	19841129
NO 164171	B	19900528		
NO 164171	C	19900905		
AU 8436028	A1	19850606	AU 1984-36028	19841129
AU 579121	B2	19881117		
JP 60149583	A2	19850807	JP 1984-250660	19841129
JP 06092389	B4	19941116		
ZA 8409331	A	19860730	ZA 1984-9331	19841129
IL 73686	A1	19880531	IL 1984-73686	19841129
PL 146377	B1	19890131	PL 1984-250633	19841129
HU 35677	O	19850729	HU 1984-4444	19841130

	HU 199837	B	19900328		
	RO 90414	B3	19861210	RO 1984-116474	19841130
	US 4888426	A	19891219	US 1987-56200	19870601
	SU 1694064	A3	19911123	SU 1987-4203318	19870917
	CA 1330081	A1	19940607	CA 1988-564954	19880422
	FI 8804037	A	19880901	FI 1988-4037	19880901
	FI 84070	B	19910628		
	FI 84070	C	19911010		
	US 5025014	A	19910618	US 1989-447312	19891207
	US 5126339	A	19920630	US 1991-671338	19910319
PRAI	US 1983-556742		19831130		
	US 1984-660608		19841012		
	EP 1984-201611		19841107		
	CA 1984-468587		19841126		
	FI 1984-4708		19841129		
	US 1987-56200		19870601		
	US 1989-447312		19891207		

OS CASREACT 104:68856

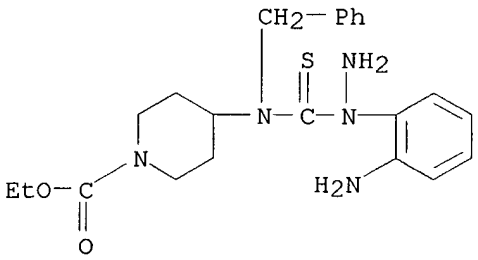
GI For diagram(s), see printed CA Issue.

AB The title compds. [I; R = H, cycloalkyl, pyridinyl, pyrazinyl, alkyl-(un)substituted furanyl, thiazolyl, imidazolyl, halo-(un)substituted thienyl, (un)substituted alkyl, Ph; R1 = H, alkyl, cycloalkyl, alkanoyl, alkoxycarbonyl, (un)substituted phenylalkyl; R2 = H, alkyl; R3 = alkyl, pyrrolidinyl, piperidinyl, homopiperonyl, each substituted by a group contg. a bicyclic heterocyclic moiety; X = atoms required to complete an (un)substituted C6H6 or pyridine ring] (>150 in all) were prepd. Thus, 1-[(4-fluorophenyl)methyl]-N-(4-piperidinyl)-1H-benzimidazol-2-amine was alkylated by heating at 70.degree. with 6-(2-bromoethyl)-3,7-dimethyl-5H-thiazolo[3,2-a]pyrimidin-5-one-HBr in DMF contg. Na2CO3 to give 62.8% II. II had antihistaminic activity in rats, counteracting the lethality of compd. 48/80 with an ED50 of 0.31 mg/kg s.c. or orally, and inhibiting gastric lesions caused by the same agent with an ED50 of 0.63 mg/kg orally.

IT **99158-21-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclization of)

RN 99158-21-1 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[1-(2-aminophenyl)hydrazino]thioxomethyl](phenylmethyl)amino]-, ethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 25 OF 29 HCAPLUS COPYRIGHT 2002 ACS

AN 1984:423473 HCAPLUS

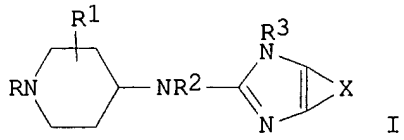
DN 101:23473

TI N-(Bicyclic heterocyclyl)-4-piperidinamines

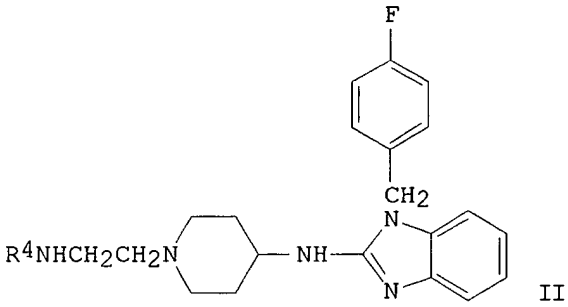
IN Janssens, Frans Eduard; Torremans, Joseph Leo Ghislanus; Hens, Jozef Francis; Van Offenwert, Theophilus Theresia J. M.
PA Janssen Pharmaceutica N. V., Belg.
SO Eur. Pat. Appl., 87 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 99139	A2	19840125	EP 1983-200832	19830608
	EP 99139	A3	19840222		
	EP 99139	B1	19870211		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	US 4556660	A	19851203	US 1983-487774	19830422
	IN 156065	A	19850504	IN 1983-CA599	19830512
	CA 1266267	A1	19900227	CA 1983-429869	19830607
	AT 25459	E	19870215	AT 1983-200832	19830608
	SU 1297728	A3	19870315	SU 1983-3608869	19830627
	FI 8302521	A	19840113	FI 1983-2521	19830711
	FI 78480	B	19890428		
	FI 78480	C	19890810		
	DK 8303185	A	19840113	DK 1983-3185	19830711
	NO 8302524	A	19840113	NO 1983-2524	19830711
	NO 160850	B	19890227		
	NO 160850	C	19890607		
	JP 59021680	A2	19840203	JP 1983-124900	19830711
	HU 32108	O	19840628	HU 1983-2471	19830711
	HU 203550	B	19910828		
	AU 8316728	A1	19850117	AU 1983-16728	19830711
	AU 563363	B2	19870709		
	ZA 8305044	A	19850227	ZA 1983-5044	19830711
	RO 87533	B3	19851031	RO 1983-111600	19830711
	ES 524029	A1	19851116	ES 1983-524029	19830711
	IL 69198	A1	19870130	IL 1983-69198	19830711
	PL 147092	B1	19890429	PL 1983-242970	19830712
	US 4760074	A	19880726	US 1985-800587	19851121
	US 4820822	A	19890411	US 1987-115272	19871102
	US 33833	E	19920225	US 1990-619558	19901129
PRAI	US 1982-397626		19820712		
	US 1983-487774		19830422		
	EP 1983-200832		19830608		
	US 1985-800587		19851121		
	US 1987-115272		19871102		

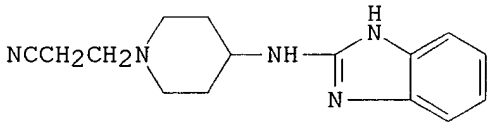
OS CASREACT 101:23473
GI



I



II



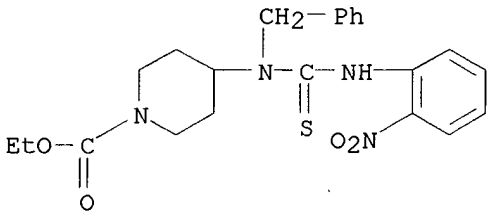
IV

AB About 100 antihistaminic title compds. I [R = substituted piperidinyl, substituted alkyl; R1 = H, alkyl; R2 = H, alkyl, cycloalkyl, acyl, aralkyl; R3 = H, (un)substituted alkyl, cycloalkyl, aryl; X = CH:CHCH:CH, N:CHCH:CH, CH:NCH:CH, CH:CHN:CH, CH:CHCH:N] were prepd. Thus N-piperidinylbenzimidazolamine II (R4 = 2-pyrimidinyl)(III) was prepd. from 2-chloropyrimidine and II (R4 = H), which was prepd. from N-piperidinylbenzimidazolamine IV. III had an ED50 of 0.63 mg/kg s.c. against stomach lesions induced by vasoactive amines in rats.

IT **90518-50-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrogenation of)

RN 90518-50-6 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[[(2-nitrophenyl)amino]thioxomethyl](phenylmethyl)amino]-, ethyl ester (9CI) (CA INDEX NAME)



L17 ANSWER 26 OF 29 HCAPLUS COPYRIGHT 2002 ACS

AN 1981:30579 HCAPLUS

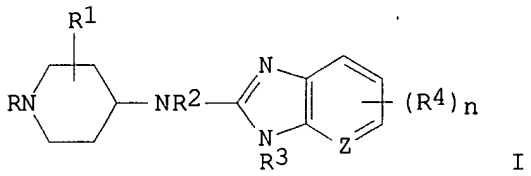
DN 94:30579

TI N-Heterocyclyl-4-piperidinamines

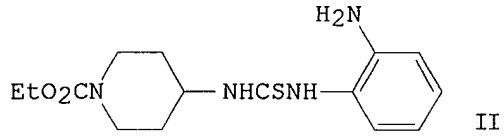
IN Janssens, Frans; Luyckx, Marcel; Stokbroekx, Raymond; Torremans, Joseph
PA Janssen Pharmaceutica N. V., Belg.
SO U.S., 27 pp. Cont.-in-part of U.S. Ser. No. 892,534, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4219559	A	19800826	US 1979-2276	19790110
	CA 1140119	A1	19830125	CA 1979-323763	19790319
	AU 7945296	A1	19791018	AU 1979-45296	19790321
	AU 523352	B2	19820722		
	DK 7901298	A	19791004	DK 1979-1298	19790329
	DK 169325	B1	19941010		
	EP 5318	A1	19791114	EP 1979-300525	19790330
	EP 5318	B1	19820106		
	R: BE, CH, DE, FR, GB, IT, LU, NL, SE				
	RO 79320	P	19820817	RO 1979-97082	19790330
	NO 7901097	A	19791004	NO 1979-1097	19790402
	NO 154058	B	19860401		
	NO 154058	C	19860709		
	FI 7901084	A	19791004	FI 1979-1084	19790402
	FI 64801	B	19830930		
	FI 64801	C	19840110		
	JP 54151982	A2	19791129	JP 1979-38447	19790402
	JP 01001477	B4	19890111		
	ES 479206	A1	19791216	ES 1979-479206	19790402
	ZA 7901557	A	19801126	ZA 1979-1557	19790402
	IL 56992	A1	19830331	IL 1979-56992	19790402
	AT 7902425	A	19830715	AT 1979-2425	19790402
	AT 373887	B	19840227		
	CS 256358	B2	19880415	CS 1979-2227	19790402
	CS 256380	B4	19880415	CS 1984-3451	19790402
	PL 123380	B1	19821030	PL 1979-214648	19790403
	HU 25906	O	19830829	HU 1979-JA841	19790403
	HU 182965	B	19840328		
	SU 1056902	A3	19831123	SU 1979-2747000	19790403
	AT 8204538	A	19830715	AT 1982-4538	19821214
	AT 373888	B	19840227		
	DK 8300831	A	19830224	DK 1983-831	19830224
	DK 171841	B1	19970630		
	ES 524224	A3	19841216	ES 1983-524224	19830719
	NO 8402563	A	19791004	NO 1984-2563	19840625
	NO 154090	B	19860407		
	NO 154090	C	19860716		
	ES 542804	A3	19851216	ES 1985-542804	19850503
	JP 01117880	A2	19890510	JP 1988-144898	19880614
	JP 02040666	B4	19900912		
PRAI	US 1978-892534		19780403		
	US 1979-2276		19790110		
	US 1979-2279		19790110		
	DK 1979-1298		19790329		
	AT 1979-2425		19790402		

GI



I



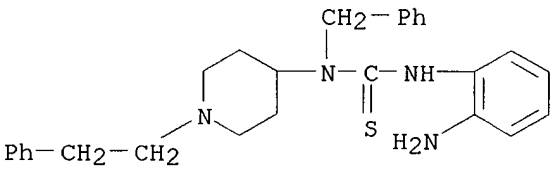
II

AB 1-(4-Piperidinyl)-3-(2-aminophenyl)thioureas and heteroarom. analogs underwent cyclocondensation to give title compds. I [R = alkyl, halo-, hydroxy-, cyano-, isothiocyanato-, alkoxy-, aryl-, heteroaryl-, aryloxy-, (heteroaryl)oxy-, arylthio-, (heteroaryl)thio-, arylsulfonyl-, (heteroaryl)sulfonyl-, or aminoalkyl, alkenyl, aryl- or (heteroaryl)alkenyl, cycloalkyl, cyanocycloalkyl, aryl- or (heteroaryl)cycloalkyl, a 1H-benzimidazol-2-yl group, R5CmH2m [m = 1-6; R5 = a 4,5-dihydro-5-oxo-1H-tetrazol-1-yl group, 2,3-dihydro-1,4-benzodioxin-6-yl, 2,3-dihydro-2-oxo-1H-benzimidazol-1-yl, 2,3-dihydro-3-oxo-4H-1,4-benzoxazin-4-yl, (10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-ylidene)methyl, 4-morpholinyl, 1-piperidinyl, 1-pyrrolidinyl, mono- or disubstituted amino]; R1 = H, alkyl; R2 = H, alkyl, cycloalkyl, aryl- or (heteroaryl)alkyl, alkanoyl; R3 = H, alkyl, aryl- or (heteroaryl)cycloalkyl, aryl- or (heteroaryl)alkyl, diaryl- or bis(heteroaryl)alkyl; Z = CH, N; n = 0, 1, 2; R4 = halo, alkyl, alkoxy, CF3], useful as antihistaminics (no data). A mixt. of thiourea II and MeI in EtOH was refluxed 8 h to yield I (R = CO2Et, Z = CH, n = 0, R1 = R2 = R3 = H), the latter was converted to the resp. I (R = H), and the product was N-alkylated to give I (R = PhCH2CH2, Z = CH, n = 0, R1 = R2 = R3 = H).

IT **73733-97-8**
RL: RCT (Reactant)
(cyclocondensation reaction of)

RN 73733-97-8 HCAPLUS

CN Thiourea, N'-(2-aminophenyl)-N-[1-(2-phenylethyl)-4-piperidinyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



L17 ANSWER 27 OF 29 HCAPLUS COPYRIGHT 2002 ACS

AN 1980:215439 HCAPLUS

DN 92:215439

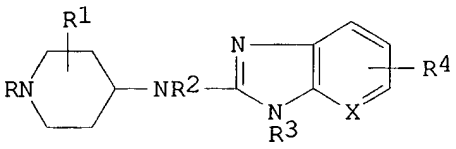
TI N-Heterocyclyl-4-piperidinamines and pharmaceutical compositions comprising them

IN Janssens, Frans; Stokbroekx, Raymond; Torremans, Joseph; Luyckx, Marcel

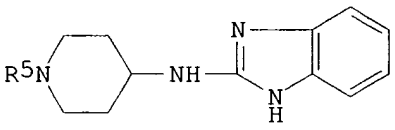
PA Janssen Pharmaceutica N.V., Belg.
SO Eur. Pat. Appl., 100 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 5318	A1	19791114	EP 1979-300525	19790330
	EP 5318	B1	19820106		
	R: BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4219559	A	19800826	US 1979-2276	19790110
	CS 256358	B2	19880415	CS 1979-2227	19790402
	CS 256380	B4	19880415	CS 1984-3451	19790402
PRAI	US 1978-892534		19780403		
	US 1979-2276		19790110		
	US 1979-2279		19790110		

GI



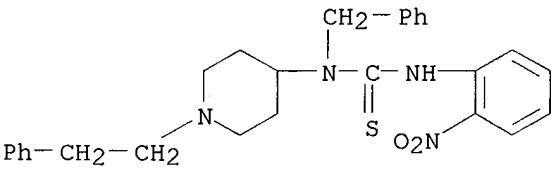
I



II

AB Antihistaminic (no data) piperidinylaminoimidazoles I (X = CH, N; R = optionally substituted alkyl, alkenyl, aralkyl, 1-aralkyl-2-benzimidazolyl; R1 = H, alkyl; R2 = H, alkyl, cycloalkyl, aralkyl, alkanoyl; R3 = H, alkyl, aryl, cycloalkyl, aralkyl; R4 = halogen, alkyl, aylkoxy, CF3) were prepd. Thus, II (R5 = CH2CH2OPh) was obtained in 70% yield by treating II (R5 = H) with BrCH2CH2OPh.

IT **73733-87-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 73733-87-6 HCAPLUS
CN Thiourea, N'-(2-nitrophenyl)-N-[1-(2-phenylethyl)-4-piperidinyl]-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

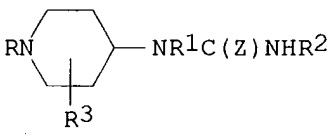


L17 ANSWER 28 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1978:22640 HCAPLUS
DN 88:22640
TI Urea and thiourea derivatives
IN Arimura, Katsuo; Konishi, Mitsuhiro
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan

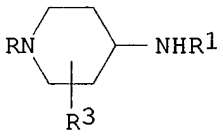
SO Japan. Kokai, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 52085174	A2	19770715	JP 1976-1029	19760105

GI



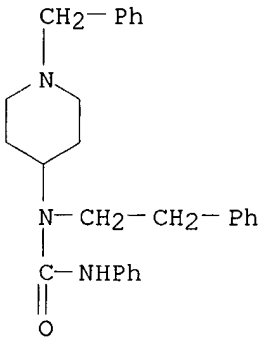
I



II

AB One hundred and forty-five title derivs. I (R = H, alkyl, alkenyl, etc.; R1 = aralkyl, aryl, naphthyl, etc.; R2 = alkyl, cycloalkyl, alkenyl, etc.; R3 = H, alkyl; Z = O, S) or their salts were prepd., e.g., by reaction of II with R2N:C:Z. I are useful as analgesics not antagonized by levallorphan. Thus, 2.4 g PhNCO was added to 5.3 g II (R = PhCH2, R1 = Ph, R3 = H) in C6H6 and the mixt. refluxed 2.5 h to give 5.1 g I (R = PhCH2, R1 = R2 = Ph, R3 = H, Z = O).

IT **59628-14-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 59628-14-7 HCAPLUS
CN Urea, N'-phenyl-N-(2-phenylethyl)-N-[1-(phenylmethyl)-4-piperidinyl]-(9CI) (CA INDEX NAME)

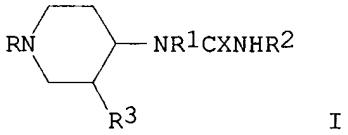


L17 ANSWER 29 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 1976:432864 HCAPLUS
DN 85:32864
TI 4-Piperidylurea and -thiourea derivatives
IN Arimura, Katsuo; Konishi, Mitsuhiro
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan

SO Ger. Offen., 21 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2545501	A1	19760422	DE 1975-2545501	19751010
	JP 51052176	A2	19760508	JP 1974-117503	19741012
	BE 834247	A1	19760202	BE 1975-160739	19751006
	NL 7511857	A	19760414	NL 1975-11857	19751009
	SE 7511408	A	19760413	SE 1975-11408	19751010
	AU 7585643	A1	19770421	AU 1975-85643	19751010
	FR 2287228	A1	19760507	FR 1975-31221	19751013
PRAI	JP 1974-117503		19741012		

GI



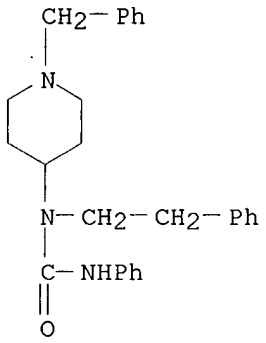
I

AB Piperidylureas I (R = Me, aralkyl, substituted aralkyl, Ac, Bz, EtO2C; R1 = Me, Ph, substituted phenyl, furfuryl, thenyl, pyridyl, naphthyl; R2 = C1-3 alkyl, allyl, Ph, substituted phenyl; R3 = H, Me; X = O, S) (78 compds.) were prepd. by treating 4-aminopiperidines with R2NCX or by substitution on I (R = H). I are non-narcotic analgesics. Thus, I (R = CH2CH2Ph, R1 = R2 = Ph, R3 = H, X = S) has an i.p. ED50 in the electroshock test of 10 mg/kg.

IT **59628-14-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 59628-14-7 HCAPLUS

CN Urea, N'-phenyl-N-(2-phenylethyl)-N-[1-(phenylmethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



Inventor Search

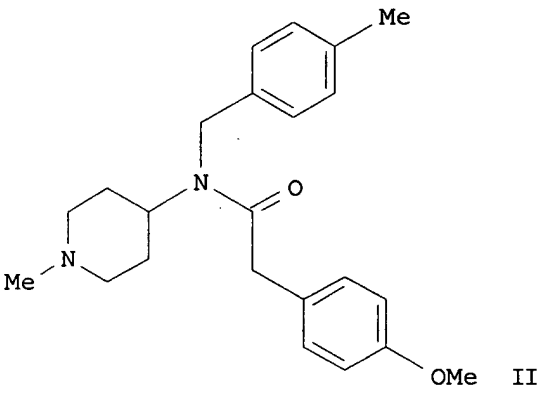
L13 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:711671 HCAPLUS
TI 5-hydroxytryptamine2A receptor inverse agonists as antipsychotics
AU Weiner, D. M.; Burstein, E. S.; Nash, N.; **Croston, G. E.**; Currier, E. A.; Vanover, K. E.; Harvey, S. C.; Donohue, E.; Hansen, H. C.; **Andersson, C. M.**; Spalding, T. A.; Gibson, D. F. C.; Krebs-Thomson, K.; Powell, S. B.; Geyer, M. A.; Hacksell, U.; Brann, M. R.
CS ACADIA Pharmaceuticals Inc., San Diego, CA, USA
SO J. Pharmacol. Exp. Ther. (2001), 299(1), 268-276
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB We have used a cell-based functional assay to define the pharmacol. profiles of a wide range of central nervous system active compds. as agonists, competitive antagonists, and inverse agonists at almost all known **monoaminergic** G-protein-coupled receptor (GPCR) subtypes. Detailed profiling of 40 antipsychotics confirmed that as expected, most of these agents are potent competitive antagonists of the dopamine D2 receptor. Surprisingly, this anal. also revealed that most are potent and fully efficacious 5-hydroxytryptamine (5-HT)2A receptor inverse agonists. No other mol. property was shared as universally by this class of compds. Furthermore, comparisons of receptor potencies revealed that antipsychotics with the highest extrapyramidal side effects (EPS) liability are significantly more potent at D2 receptors, the EPS-sparing atypical agents had relatively higher potencies at **5-HT2A** receptors, while three were significantly more potent at **5-HT2A** receptors. Functional high-throughput screening of a diverse chem. library identified 530 ligands with inverse agonist activity at **5-HT2A** receptors, including several series of compds. related to known antipsychotics, as well as a no. of novel chemistries. An analog of one of the novel chem. series, AC-90179, was pharmacol. profiled against the remaining **monoaminergic** GPCRs and found to be a highly selective **5-HT2A** receptor inverse agonist. The behavioral pharmacol. of AC-90179 is characteristic of an atypical antipsychotic agent.
RE.CNT 41
RE
(1) Arranz, M; Lancet 2000, V355, P1615 HCAPLUS
(3) Bakshi, V; J Pharmacol Exp Ther 1994, V271, P787 HCAPLUS
(4) Birnbaumer, M; J Recept Signal Transduct Res 1995, V15, P131 HCAPLUS
(5) Blakely, R; J Exp Biol 1994, V196, P263 HCAPLUS
(6) Bond, R; Nature (Lond) 1995, V374, P272 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:676749 HCAPLUS
DN 135:242140
TI Preparation of N-piperidinyl-N-alkyl-acetamides and N,N,N'-substituted ureas as **5-HT2A** inverse agonists/antagonists
IN **Andersson, Carl M.; Croston, Glenn; Hansen, E. L.; Uldam, A. K.**
PA Acadia Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001066521	A1	20010913	WO 2001-US7187	20010306
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002004513	A1	20020110	US 2001-800096	20010306
PRAI	US 2000-187289	P	20000306		

OS MARPAT 135:242140
GI



II

AB Title compds. Ar1-Y2-Y1-N(Z)-C:W-X1-X2-Ar2 [Z = NR-substituted piperidinyl, tropanyl,azetidinyl, etc.; R = H, cyclic/straight-chain acyclic organyl group, hydroxyalkyl, aminoalkyl, aralkyl or heteroaralkyl group; X1 = CH2, vinylene, NH or N-alkyl; X2 = CH2, or, when X1 = CH2 or vinylene, X2 = CH2 or a bond; or when X1 is CH2, X2 = O, S, NH, N(lower alkyl) or a bond; Y1 = CH2 and Y2 = CH2, vinylene, ethylene, propylene, bond; or Y1 = bond and Y2 = vinylene; or Y1 = ethylene and Y2 = O, S, NH, N(lower alkyl); Ar1 and Ar2 = (un)substituted (hetero)aryl provided that Ar1 and Ar2 are not simultaneously phenyl; W = O, S; I] were prepd. Examples include over 130 compds. synthesized, 5 serotonin receptor binding assays and 3 in-vivo models. For instance, 4-methylbenzylamine was reductively alkylated with 1-methyl-4-piperidone (MeOH, HOAc, NaCNBH3, 20 h., room temp.). The resulting amine was alkylated with 4-methoxyphenylacetyl chloride (DCM, 4 h., room temp.) to give II, isolated as the hydrochloride salt and subsequently purified by chromatog. Many of the examples had pIC50 (-log IC50) = 7.8 - 9.0 for HT2A. I are used for the treatment of disease in which modification of serotonergic receptor activity has a beneficial effect.

RE.CNT 2
RE

(1) King, F; US 4853394 A 1989 HCAPLUS
(2) Lundbeck & Co As H; EP 0260070 A 1988 HCAPLUS

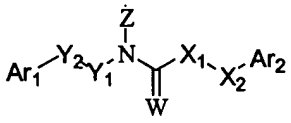
L13 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:840645 HCAPLUS
DN 134:100742
TI Multistep solution-phase parallel synthesis of spiperone analogs
AU Hansen, Henrik C.; Olsson, Roger; **Croston, Glenn**; **Andersson, Carl-Magnus**
CS Synthetic Chemistry, ACADIA Pharmaceuticals A/S, Glostrup, DK-2600, Den.
SO Bioorganic & Medicinal Chemistry Letters (2000), 10(21), 2435-2439
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB A flexible, multistep parallel synthesis of spiperone analogs is described. A library of 4-substituted piperidines, assembled utilizing reductive amination and acylation protocols, was alkylated either homogeneously or heterogeneously, exploiting a product release only concept, to afford an oxa-series of spiperone analogs. Screening of the products at 5-HT2 and D2 receptors revealed **5-HT2A** antagonists with improved selectivity compared to spiperone and AMI-193.
RE.CNT 11
RE
(2) Brann, M; US 5707798 1998 HCAPLUS
(3) Ismaiel, A; J Med Chem 1993, V36, P2519 HCAPLUS
(4) Lever, J; Life Sci 1990, V46, P1967 HCAPLUS
(5) Mach, R; J Med Chem 1992, V35, P423 HCAPLUS
(7) Metwally, K; J Med Chem 1998, V41, P5084 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d que

L12 1240 SEA FILE=HCAPLUS ABB=ON PLU=ON ANDERSSON C?/AU OR CROSTON G?/AU OR HANSEN E?/AU OR ULDAM A?/AU
L13 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L12 AND (MONOAMINERG? OR SERORONERG? OR 5HT OR 5(W)HT2A)

We Claim:

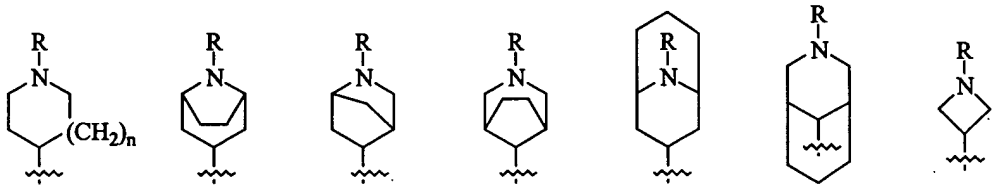
1. A compound of formula (I)



I

wherein

Z is



, , , , , or

in which

R is a hydrogen, a cyclic or straight-chained or branched acyclic organyl group, a lower hydroxyalkyl group, a lower aminoalkyl group, or an aralkyl or heteroaralkyl group;

n is 0, 1, or 2;

X_1 is methylene, vinylene, or an NH or N(lower alkyl) group; and

X_2 is methylene, or, when X_1 is methylene or vinylene, X_2 is methylene or a bond; or when X_1 is methylene, X_2 is O, S, NH, or N(lower alkyl) or a bond;

Y_1 is methylene and Y_2 is methylene, vinylene, ethylene, propylene, or a bond;

or

~~Y_1 is a bond and Y_2 is vinylene;~~ or

Y_1 is ethylene and Y_2 is O, S, NH, or N(lower alkyl);

Ar_1 and Ar_2 independently are unsubstituted or substituted aryl or heteroaryl groups, provided that Ar_1 and Ar_2 are not simultaneously phenyl; and

W is oxygen or sulfur.

2. A compound according to claim 1, wherein

Y_1 is methylene and Y_2 is a bond, methylene, ethylene, or vinylene; or

Y_1 is ethylene and Y_2 is O or S;

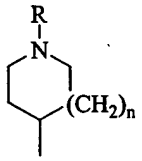
and

X_1 is methylene and X_2 is a bond, methylene, O, or S; or

X_1 is NH or N(lower alkyl) and X_2 is methylene.

3. A compound according to claim 2, wherein

Z is



and W is oxygen.

4. A compound according to claim 3, wherein

Ar_1 and Ar_2 independently are mono- or disubstituted phenyl groups.

5. A compound according to claim 4, wherein

R is a hydrogen, a lower alkyl group, a cyclic organyl group, or a substituted or unsubstituted aralkyl or heteroaralkyl group;

n is 1;

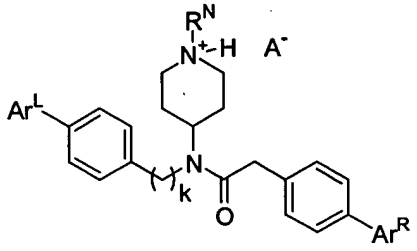
Y_1 is methylene, Y_2 is a bond, methylene, ethylene, or vinylene;

X_1 is methylene and X_2 is a bond, or.

X_1 is NH or N(lower alkyl) and X_2 is methylene; and

Ar_1 and Ar_2 are phenyl groups, independently *p*-substituted with groups selected from lower alkyl, lower alkoxy and halogen.

6. A compound according to claim 1, having a formula (II)



II

wherein R^N is hydrogen, lower alkyl, aralkyl, or heteroaralkyl;

Ar^L is selected from lower alkyl, lower alkoxy and halogen

Ar^R is selected from lower alkyl, lower alkoxy and halogen;

k is 1 or 2

and A^- is a suitable anion.

7. The compound according to claim 1, wherein the compound is selected from the group consisting of:

N-(1-(1-methylethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(2,2-dimethylethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-pentylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-hexylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-cyclohexylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-cyclopentylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-cyclobutylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-cyclopropylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(cyclopentylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(cyclobutylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(cyclopropylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(2-hydroxyethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(3-hydroxypropyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-*N*-(piperidin-4-yl)-*N'*-phenylmethylcarbamide;

N-((4-methylphenyl)methyl)-*N*-(1-(2-methylpropyl)piperidin-4-yl)-*N'*-phenylmethylcarbamide;

N-(1-((2-bromophenyl)methyl)piperidin-4-yl)-*N*-((4-methylphenyl)methyl)-*N'*-phenylmethylcarbamide;

N-(1-((4-hydroxy-3-methoxyphenyl)methyl)piperidin-4-yl)-*N*-((4-methylphenyl)methyl)-*N'*-phenylmethylcarbamide;

N-(1-((5-ethylthien-2-yl)methyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-N'-phenylmethylcarbamide;

N-(1-(imidazol-2-ylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-N'-phenylmethylcarbamide;

N-(1-(cyclohexylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-N'-phenylmethylcarbamide;

N-(1-((4-fluorophenyl)methyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-N'-phenylmethylcarbamide;

N-((4-methylphenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-methylpiperidin-4-yl)-4-methoxyphenylacetamide;

N-(1-ethylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-propylpiperidin-4-yl)-4-methoxyphenylacetamide;

N-(1-butylpiperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(3,3-dimethylbutyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-(cyclohexylmethyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-(2-methylpropyl)piperidin-4-yl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-((4-methylphenyl)methyl)piperidin-4-yl)-4-methoxyphenylacetamide;

N-(1-((4-hydroxyphenyl)methyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(1-((2-hydroxyphenyl)methyl)piperidin-4-yl)-N-((4-methylphenyl)methyl)-4-methoxyphenylacetamide;

N-(3-phenylpropyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-(2-phenylethyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((2-methoxyphenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((2-chlorophenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((3,4-di-methoxyphenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((4-fluorophenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((2,4-di-chlorophenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((3-methylphenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-((3-bromophenyl)methyl)-N-(piperidin-4-yl)-4-methoxyphenylacetamide;

N-(1-(phenylmethyl)piperidin-4-yl)-N-(3-phenyl-2-propen-1-yl)-4-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-phenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-3-phenylpropionamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-(phenylthio)acetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-phenoxyacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-(4-chlorophenoxy)acetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-3-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-4-fluorophenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-2,5-di-methoxyphenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-piperidin-4-yl)-4-chlorophenylacetamide;

N-((4-methylphenyl)methyl)-N-(1-(phenylmethyl)pyrrolidin-3-yl)-N'-phenylmethylcarbamide;

N-((4-methylphenyl)methyl)-N-(1-(phenylmethyl)pyrrolidin-3-yl)-4-methoxyphenylacetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-(piperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-(1-ethylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-chlorbenzyl)-*N*-(1-ethylpiperidin-4-yl) acetamide.

2-(4-methoxyphenyl)-*N*-(4-chlorbenzyl)-*N*-(1-isopropylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-chlorobenzyl)-*N*-(piperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-chlorbenzyl)-*N*-(1-cyclopentylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-chlorbenzyl)-*N*-(1-isopropylpiperidin-4-yl) acetamide;

2-(phenyl)-*N*-(4-trifluoromethylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-fluorophenyl)-*N*-(4-trifluoromethylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-*N*-(4-trifluoromethylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Trifluoromethylphenyl)-*N*-(4-trifluoromethylbenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Fluorophenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(phenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Trifluoromethylphenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-trifluoromethylphenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-Phenyl-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Chlorophenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-trifluoromethylphenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-Phenyl-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Chlorophenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-*N*-[4-(methoxycarbonyl)benzyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4 methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(4-chloromethyl-2-thiazolylmethyl) piperidin-4-yl] acetamide;

2-(4 methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[3(1,3 dihydro-2H-benzimidazol-2-on-1-yl) propyl] piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(2-4(fluorophenyl) ethyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(2,5-dimethoxyphenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(2,4-dichlorophenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(3-chlorophenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(4-methoxyphenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-[2-(3-fluorophenyl) ethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-ethoxyphenyl)-*N*-[2-(4-fluorophenethyl]-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-ethoxyphenyl)-*N*-(4-fluorobenzyl)-*N*-(1-methylpiperidin-4-yl) acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[2-(2-hydroxyethoxy)ethyl] piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-((2-chloro-5-thienyl)methyl) piperidin-4-yl] acetamide;

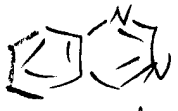
2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(2-(imidazolidinon-1-yl)ethyl)piperidin-4-yl] acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[2-(2,4(1H,3H)quinazolinedion-3-yl)ethyl] piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[2-(1,3-dioxolan-2-yl)ethyl]piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[2-(3-indolyl)ethyl] piperidin-4-yl} acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-{1-[3-(1,2,4-triazol-1-yl)propyl]piperidin-4-yl} acetamide;



504

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(5-benzofurazanylmethyl)piperidin-4-yl] acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(5-chlorobenzo[b]thien-3-ylmethyl) piperidin-4-yl] acetamide;

2-(4-methoxyphenyl)-*N*-(4-methylbenzyl)-*N*-[1-(5-phenyl-1,2,4-oxadiazol-3-ylmethyl)piperidin-4-yl] acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-isopropylpiperidin-4-yl)-acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-ethylpiperidin-4-yl)-acetamide;

2-Phenyl-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide,2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-cyclopentylpiperidin-4-yl)-acetamide;

2-(4-Fluorophenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-(2-hydroxyethyl)-piperidin-4-yl)-acetamide;

2-(4-Chlorophenyl)-N-(4-methylbenzyl)-N-(1-cyclobutylpiperidin-4-yl)-acetamide;

2-(4-Methoxyphenyl)-N-(4-methylbenzyl)-N-(1-cyclobutylpiperidin-4-yl)-acetamide,2-(4-Methoxyphenyl)-N-(4-methylbenzyl)-N-(tropin-4-yl)-acetamide;

N-(4-Methylbenzyl)-N-(1-methylpiperidin-4-yl)-N′-benzyl-carbamide;

N-(4-Methylbenzyl)-N-(1-methylpiperidin-4-yl)-N′-phenyl-carbamide;

N-Phenethyl-N-(1-methylpiperidin-4-yl)-N′-benzyl-carbamide;

2-Phenyl-N-(4-methoxybenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Trifluoromethylphenyl)-N-(4-methoxybenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Fluorophenyl)-N-(4-methoxybenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Methoxyphenyl)-N-(4-methoxybenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Methylphenyl)-N-(4-chlorobenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

2-(4-Hydroxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-acetamide;

N-Phenethyl-N-(1-methylpiperidin-4-yl)-N′-phenyl-carbamide;

N-(3-Phenylpropyl)-N-(1-methylpiperidin-4-yl)-N′-benzyl-carbamide;

N-(3-Phenylpropyl)-N-(1-methylpiperidin-4-yl)-N′-phenyl-carbamide;

2-(4-Methoxyphenyl)-2,2-ethylene-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-N-alpha-methylbenzyl-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-N-(4-methylbenzyl)-N-(3-tropen-4-yl) acetamide;

2-Phenyl-2-ethyl-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

N-Phenethyl-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl)-amine;

2-(4-Methoxyphenyl)-N-(1-indanyl)-N-(1-methylpiperidin-4-yl) acetamide;

N-(4-Methylbenzyl)-N-(1-methylpiperidin-4-yl)-N′-(4-methoxybenzyl)-carbamide;

2-(3,4-dimethoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(3,4-Methylenedioxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Methoxyphenyl)-N-(4-methylbenzyl)-N-(1-t-butylpiperidin-4-yl)-acetamide;

N-(4-Methylbenzyl)-N-(1-methylpiperidin-4-yl)-N′-phenethyl-carbamide;

N-Phenethyl-N-(1-methylpiperidin-4-yl)-N′-phenethyl-carbamide;

N-(4-Methylbenzyl)-N-(1-t-butylpiperidin-4-yl)-N′-(4-methoxybenzyl)-carbamide;

2-(4-Ethoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Butoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-i-Propoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-t-Butoxyphenyl)-N-(4-methylbenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

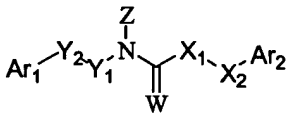
2-(4-Butoxyphenyl)-N-(4-fluorobenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-Propoxyphenyl)-N-(4-flourobenzyl)-N-(1-methylpiperidin-4-yl) acetamide;

2-(4-i-Propoxyphenyl)-N-(4-fluorobenzyl)-N-(1-methylpiperidin-4-yl) acetamide; and

2-(4-t-Butoxyphenyl)-N-(4-fluorobenzyl)-N-(1-methylpiperidin-4-yl) acetamide.

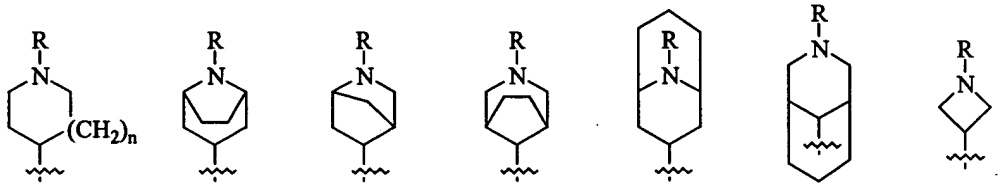
8. A compound of formula (I)



I

wherein

Z is



, , , , , or

in which

R is a hydrogen, a cyclic or straight-chained or branched acyclic organyl group, a lower hydroxyalkyl group, a lower aminoalkyl group, or an aralkyl or heteroaralkyl group; and

n is 0, 1, or 2;

X_1 is methylene, vinylene, or an NH or N(lower alkyl) group; and

X_2 is methylene, or, when X_1 is methylene or vinylene, X_2 is methylene or a bond; or when X_1 is methylene, X_2 is O, S, NH, or N(lower alkyl) or a bond;

Y_1 is methylene and Y_2 is methylene, vinylene, ethylene, propylene, or a bond; or

Y_1 is a bond and Y_2 is vinylene; or

Y_1 is ethylene and Y_2 is O, S, NH, or N(lower alkyl);

Ar_1 and Ar_2 are different unsubstituted or substituted aryl or heteroaryl groups; and

W is oxygen or sulfur.

9. A compound according to claim 8, wherein

Y_1 is methylene and Y_2 is a bond, methylene, ethylene, or vinylene; or

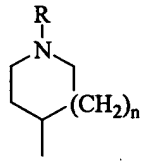
Y_1 is ethylene and Y_2 is O or S; and

X_1 is methylene and X_2 is a bond, methylene, O, or S; or

X_1 is NH or N(lower alkyl) and X_2 is a methylene .

10. A compound according to claim 9, wherein

Z is



and W is oxygen.

11. A compound according to claim 10, wherein

Ar_1 and Ar_2 independently are mono- or disubstituted phenyl groups.

12. A compound according to claim 11, wherein

R is a hydrogen, a lower alkyl group, a cyclic organyl group, or an, optionally substituted, alalkyl or heteroaralkyl group;

n is 1;

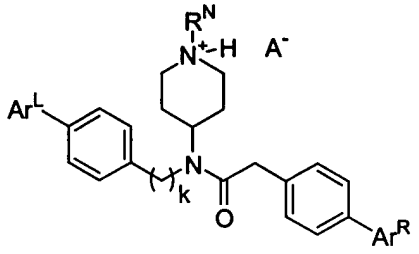
Y_1 is methylene, Y_2 is a bond, methylene, ethylene, or vinylene;

X_1 is methylene and X_2 is a bond, or

X_1 is NH or N(lower alkyl) and X_2 is methylene; and

Ar_1 and Ar_2 are phenyl groups, independently p-substituted with groups selected from alkyl, lower alkoxy and halogen.

13. A compound according to claim 7, having a formula (II):



II

wherein R^N is hydrogen, lower alkyl, aralkyl, or heteroaralkyl;

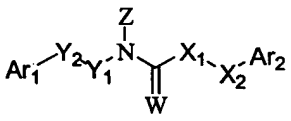
Ar^L is selected from lower alkyl, lower alkoxy and halogen

Ar^R is selected from lower alkyl, lower alkoxy and halogen;

k is 1 or 2

and A^- is a suitable anion.

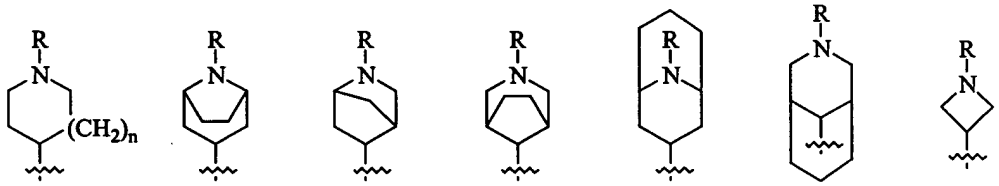
14. A pharmaceutical composition comprising an effective amount of a compound of formula (I):



I

wherein

Z is



, , , , , or

in which

R is a hydrogen, a cyclic or straight-chained or branched acyclic organyl group, a lower hydroxyalkyl group, a lower aminoalkyl group, or an aralkyl or heteroaralkyl group; and

n is 0, 1, or 2;

X_1 is methylene, vinylene, or an NH or N(lower alkyl) group; and

X_2 is methylene, or, when X_1 is methylene or vinylene, X_2 is methylene or a bond; or when X_1 is methylene, X_2 is O, S, NH, or N(lower alkyl) or a bond;

Y_1 is methylene and Y_2 is methylene, vinylene, ethylene, propylene, or a bond; or

Y_1 is a bond and Y_2 is vinylene; or

Y_1 is ethylene and Y_2 is O, S, NH, or N(lower alkyl);

Ar_1 and Ar_2 independently are unsubstituted or substituted aryl or heteroaryl groups, provided that Ar_1 and Ar_2 are not simultaneously phenyl; and

W is oxygen or sulfur;

or a pharmaceutically acceptable salt, ester or prodrug thereof, and

a pharmaceutically acceptable diluent or excipient.

15. A method of inhibiting an activity of a monoamine receptor comprising contacting the monoamine receptor or a system containing the monoamine receptor with an amount of one or more of the compounds of claim 1 that is effective in inhibiting the activity of the monoamine receptor.

16. The method of claim 15 wherein the monoamine receptor is a serotonin receptor.

17. The method of claim 16 wherein the serotonin receptor is the 5-HT2A subclass.

18. The method of claim 16 wherein the serotonin receptor is in the central nervous system.

19. The method of claim 16 wherein the serotonin receptor is in the peripheral nervous system.

20. The method of claim 16 wherein the serotonin receptor is in blood cells or platelets.

21. The method of claim 16 wherein the serotonin receptor is mutated or modified.

22. The method of claim 15 wherein the activity is signaling activity.

23. The method of claim 15 wherein the activity is constitutive.

24. The method of claim 15 wherein the activity is associated with serotonin receptor activation.

25. A method of inhibiting an activation of a monoamine receptor comprising contacting the monoamine receptor or a system containing the monoamine receptor with an amount of a compound of one or more of the compounds of claim 1 that is effective in inhibiting the activation of the monoamine receptor.

26. The method of claim 25 wherein the activation is by an agonistic agent.

27. The method of claim 26 wherein the agonistic agent is exogenous.

28. The method of claim 26 wherein the agonistic agent is endogenous.

29. The method of claim 25 wherein the activation is constitutive.

30. The method of claim 25 wherein the monoamine receptor is a serotonin receptor.

31. The method of claim 30 wherein the serotonin receptor is the 5-HT2A subclass.

32. The method of claim 30 wherein the serotonin receptor is in the central nervous system.

33. The method of claim 30 wherein the serotonin receptor is in the peripheral nervous system.

34. The method of claim 30 wherein the serotonin receptor is in blood cells or platelets.

35. The method of claim 30 wherein the serotonin receptor is mutated or modified.

36. A method of treating a disease condition associated with a monoamine receptor comprising administering to a subject in need of such treatment a therapeutically effective amount of one or more of the compounds of claim 1.

37. The method of claim 36 wherein the disease condition is selected from the group consisting of schizophrenia, psychosis, migraine, hypertension, thrombosis, vasospasm, ischemia, depression, anxiety, sleep disorders and appetite disorders.

38. The method of claim 36 wherein the disease condition is associated with dysfunction of a monoamine receptor.

39. The method of claim 36 wherein the disease condition is associated with activation of a monoamine receptor.

40. The method of claim 36 wherein the disease condition is associated with increased activity of monoamine receptor.

41. The method of claim 36 wherein the monoamine receptor is a serotonin receptor

42. The method of claim 41 wherein the serotonin receptor is the 5-HT2A subclass.

43. The method of claim 41 wherein the serotonin receptor is in the central nervous system.

44. The method of claim 41 wherein the serotonin receptor is in the peripheral nervous system.

45. The method of claim 41 wherein the serotonin receptor is in blood cells or platelets.

46. The method of claim 41 wherein the serotonin receptor is mutated or modified.

47. A method of treating schizophrenia comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of one or more of the compounds of claim 1.

48. A method of treating migraine comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of one or more of the compounds of claim 1.

49. A method of treating psychosis comprising administering to a subject in need of such treatment a therapeutically effective amount of a compound of one or more of the compounds of claim 1.

50. A method for identifying a genetic polymorphism predisposing a subject to being responsive to one or more of the compounds of claim 1, comprising:

administering to a subject a therapeutically effective amount of the compound;

measuring the response of said subject to said compound, thereby identifying a responsive subject having an ameliorated disease condition associated with a monoamine receptor; and

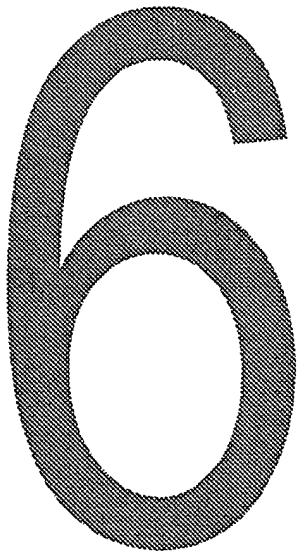
identifying a genetic polymorphism in the responsive subject, wherein the genetic polymorphism predisposes a subject to being responsive to the compound.

51. The method of claim 50 wherein the ameliorated disease condition is associated with the 5-HT class or 5-HT2A subclass of monoaminergic receptors.

52. A method for identifying a subject suitable for treatment with one or more of the compounds of claim 1, comprising detecting the presence of a polymorphism in a subject wherein the polymorphism predisposes the subject to being responsive to the compound, and wherein the presence of the polymorphism indicates that the subject is suitable for treatment with one or more of the compounds of claim 1.

UNITED STATES PATENT AND TRADEMARK OFFICE
DOCUMENT CLASSIFICATION BARCODE SHEET

Abstract



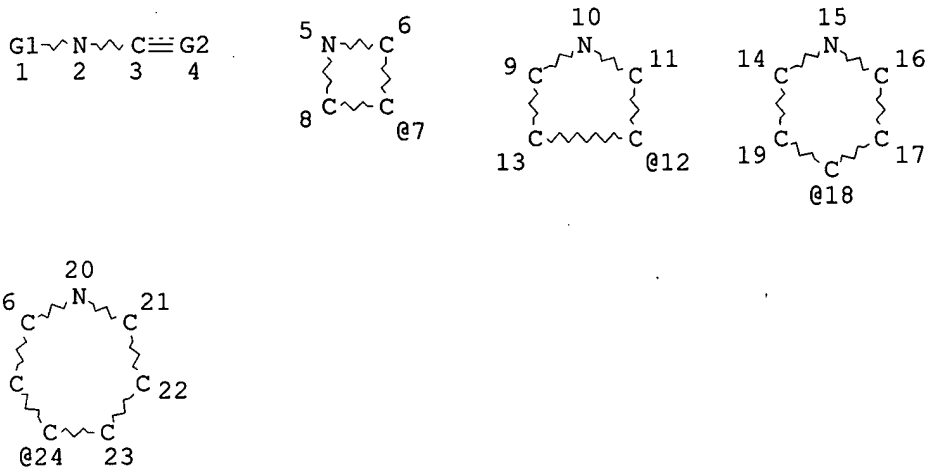
Level - 2
Version 1.1

AZACYCLIC COMPOUNDS

Abstract

Compounds and methods are provided for the treatment of disease conditions in which modification of serotonergic receptor activity has a beneficial effect. In the method, an effective amount of a compound is adminstered to a patient in need of such treatment.

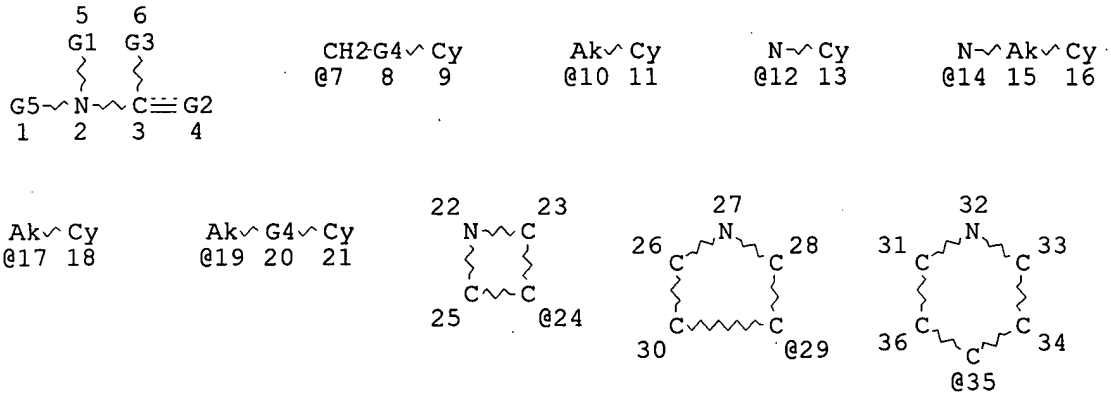
=> d que
L1 STR



VAR G1=7/12/18/24
VAR G2=O/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 26

STEREO ATTRIBUTES: NONE
L4 5463357 SEA FILE=REGISTRY ABB=ON PLU=ON NRS>2 AND NR>2
L6 124845 SEA FILE=REGISTRY SUB=L4 SSS FUL L1
L14 STR



Only inventors work had any mention of monoaminergic, 5HT, 5-HT2A, or serotonergic

Only the first substance was printed for each Reference.
Let me know if you would like to see more.

VAR G1=24/29/35/41
VAR G2=O/S
VAR G3=7/10/12/14
VAR G4=O/S/N
VAR G5=17/19
NODE ATTRIBUTES:
CONNECT IS E2 RC AT 10
CONNECT IS E2 RC AT 15
CONNECT IS E2 RC AT 17
CONNECT IS E2 RC AT 19
DEFAULT MLEVEL IS ATOM
GGCAT IS UNS AT 9
GGCAT IS LOC AT 10
GGCAT IS UNS AT 11
GGCAT IS UNS AT 13
GGCAT IS LOC AT 15
GGCAT IS UNS AT 16
GGCAT IS LOC AT 17
GGCAT IS UNS AT 18
GGCAT IS LOC AT 19
GGCAT IS UNS AT 21
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 43

STEREO ATTRIBUTES: NONE

957 substances

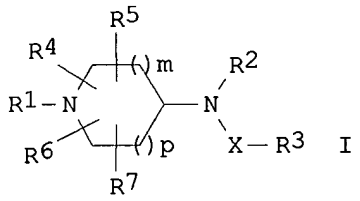
L16 957 SEA FILE=REGISTRY SUB=L6 SSS FUL L14
L17 29 SEA FILE=HCAPLUS ABB=ON PLU=ON L16 ← 29 references
L19 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND ANDERSSON?/AU
L20 28 SEA FILE=HCAPLUS ABB=ON PLU=ON L17 NOT L19

L17 ANSWER 1 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:851116 HCAPLUS
DN 135:371644
TI Pharmaceutically active piperidine derivatives, in particular as modulators of chemokine receptor activity
IN Burrows, Jeremy; Cooper, Anne; Cumming, John; Mcinally, Thomas; Tucker, Howard
PA Astrazeneca AB, Swed.
SO PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

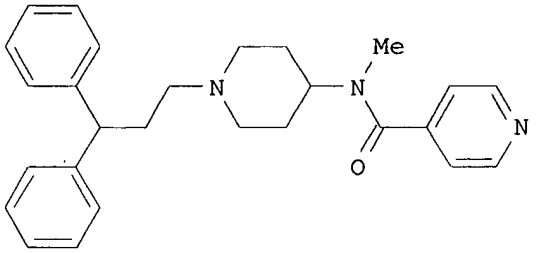
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001087839	A1	20011122	WO 2001-SE1053	20010514

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2000-11838 A 20000517
OS MARPAT 135:371644
GI



I



II

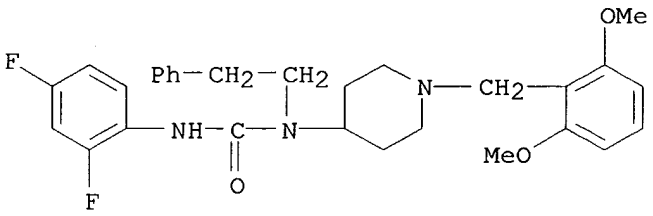
AB The title compds., e.g., [I; R1 = (un)substituted C1-6 alkyl, C3-7 cycloalkyl, C3-8 alkenyl or C3-8 alkynyl; R2 = H, C1-8 alkyl, C3-8 alkenyl, C3-8 alkynyl, C3-7 cycloalkyl, aryl, heteroaryl, heterocyclyl, aryl (C1-4)alkyl, heteroaryl(C1-4)alkyl, or heterocyclyl(C1-4)alkyl; R3 =

C1-8 alkyl, C2-8 alkenyl, mono- or disubstituted amine, C2-8 alkynyl, C3-7 cycloalkyl, C3-7 cycloalkenyl, aryl, heteroaryl, heterocyclyl, aryl (C1-4)alkyl, heteroaryl(C1-4)alkyl, or heterocyclyl(C1-4)alkyl; R4, R5, R6 and R7 = independently H, (un)substituted C1-6 alkyl, (un)substituted S(O)2NH2 or two of R4, R5, R6 and R7 can join to form, together with the ring to which they are attached, a bicyclic ring system or two of R4, R5, R6 and R7 can form an endocyclic bond; X = C(O), S(O)2, C(O)C(O), a direct bond or (un)substituted C(O)C(O)N; m and p = independently 0,1 or 2; or a pharmaceutically acceptable salt or solvate thereof], compns. comprising them, processes for prepg. then and their use in modulating CCR5 receptor activity (no data). Thus, reacting isonicotinic acid with 4-methylamino-1-(3,3-diphenylpropyl)piperidine hydrochloride (prepn. given) in the presence of diisopropylethylamine in NMP followed by a soln. of bromo-tris-pyrrolidinophosphonium hexafluorophosphate in NMP afforded II.

IT **374724-65-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutically active piperidine derivs. as modulators of chemokine receptor activity)

RN 374724-65-9 HCAPLUS

CN Urea, N'-(2,4-difluorophenyl)-N-[1-[(2,6-dimethoxyphenyl)methyl]-4-piperidinyl]-N-(2-phenylethyl)- (9CI) (CA INDEX NAME)



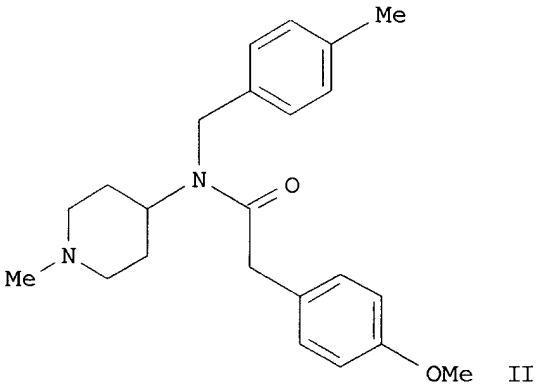
RE.CNT 20
RE
(1) Adir Et Compagnie; EP 0457686 A1 1991 HCAPLUS
(3) Archibald, J; J Med Chem 1980, V23, P857 HCAPLUS
(4) Astrazeneca Uk Limited; WO 0114333 A1 2001 HCAPLUS
(5) Bristol-Myers Squibb Company; EP 0643057 A1 1995 HCAPLUS
(7) Janssen Pharmaceutica N V; EP 0445862 A2 1991 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 2 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:676749 HCAPLUS
DN 135:242140
TI Preparation of N-piperidinyl-N-alkyl-acetamides and N,N,N'-substituted ureas as 5-HT2A inverse agonists/antagonists
IN Andersson, Carl M.; Croston, Glenn; Hansen, E. L.; Uldam, A. K. ← Inventors
PA Acadia Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001066521	A1	20010913	WO 2001-US7187	20010306
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002004513	A1	20020110	US 2001-800096	20010306
PRAI	US 2000-187289	P	20000306		

OS MARPAT 135:242140

GI



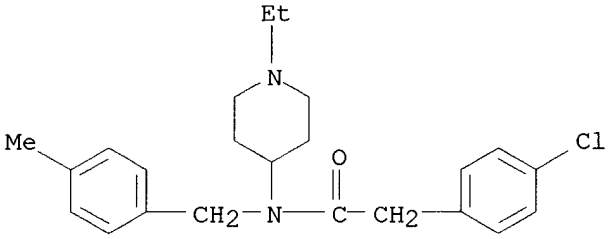
II

AB Title compds. Ar1-Y2-Y1-N(Z)-C:W-X1-X2-Ar2 [Z = NR-substituted piperidinyl, tropanyl,azetidinyl, etc.; R = H, cyclic/straight-chain acyclic organyl group, hydroxyalkyl, aminoalkyl, aralkyl or heteroaralkyl group; X1 = CH2, vinylene, NH or N-alkyl; X2 = CH2, or, when X1 = CH2 or vinylene, X2 = CH2 or a bond; or when X1 is CH2, X2 = O, S, NH, N(lower alkyl) or a bond; Y1 = CH2 and Y2 = CH2, vinylene, ethylene, propylene, bond; or Y1 = bond and Y2 = vinylene; or Y1 = ethylene and Y2 = O, S, NH, N(lower alkyl); Ar1 and Ar2 = (un)substituted (hetero)aryl provided that Ar1 and Ar2 are not simultaneously phenyl; W = O, S; I] were prepd. Examples include over 130 compds. synthesized, 5 serotonin receptor binding assays and 3 in-vivo models. For instance, 4-methylbenzylamine was reductively alkylated with 1-methyl-4-piperidone (MeOH, HOAc, NaCNBH3, 20 h., room temp.). The resulting amine was alkylated with 4-methoxyphenylacetyl chloride (DCM, 4 h., room temp.) to give II, isolated as the hydrochloride salt and subsequently purified by chromatog. Many of the examples had pIC50 (-log IC50) = 7.8 - 9.0 for HT2A. I are used for the treatment of disease in which modification of serotonergic receptor activity has a beneficial effect.

IT **359881-71-3P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug:; prepn. of N-piperidinyl-N-alkyl-aryl-acetamides and N,N,N'-substituted ureas as 5-HT2A inverse agonists)
RN 359881-71-3 HCAPLUS
CN Benzeneacetamide, 4-chloro-N-(1-ethyl-4-piperidinyl)-N-[(4-methylphenyl)methyl]-, monohydrochloride (9CI) (CA INDEX NAME)



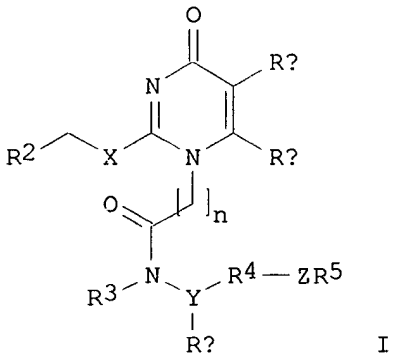
● HCl

RE.CNT 2
RE
(1) King, F; US 4853394 A 1989 HCAPLUS
(2) Lundbeck & Co As H; EP 0260070 A 1988 HCAPLUS

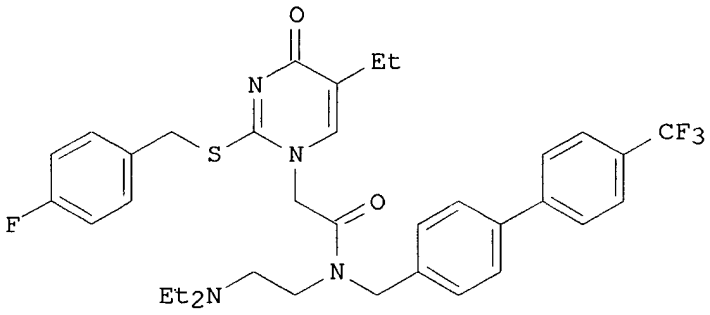
L17 ANSWER 3 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:617985 HCAPLUS
DN 135:195570
TI Preparation of pyrimidine-4-one derivatives as LDL-PLA2 inhibitors
IN Hickey, Deirdre Mary Bernadette; Ife, Robert John; Leach, Colin Andrew; Pinto, Ivan Leo; Smith, Stephen Allan; Stanway, Steven James
PA Smithkline Beecham P.L.C., UK
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001060805	A1	20010823	WO 2001-EP1515	20010213
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	GB 2000-3636	A	20000216		
	GB 2001-1437	A	20010119		

OS MARPAT 135:195570
GI



I



II

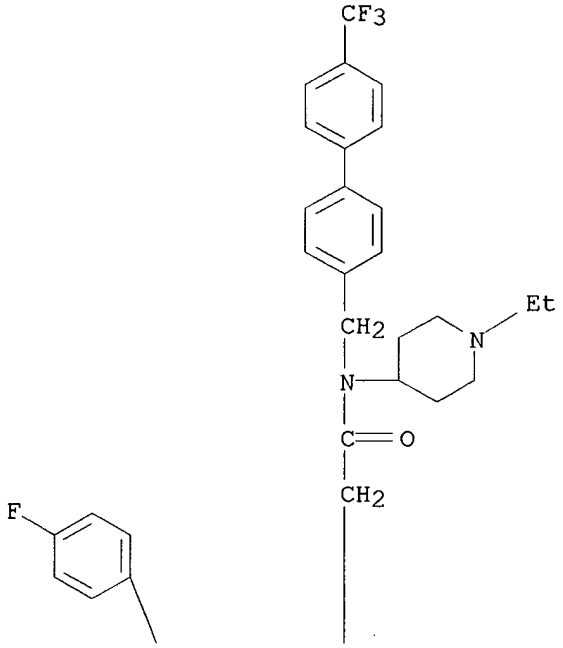
AB The title compds. [I; Ra = H, halo, alkyl, etc.; Rb = H, halo, alkyl, etc.; Ra and Rb together = (CH2)n (n = 3-4) or Ra and Rb together with the pyrimidine ring carbon atoms to which they are attached form (un)substituted fused benzo or heteroaryl ring; Rc = H, alkyl; R2 = (un)substituted (hetero)aryl; R3 = H, alkyl, halo, etc.; R4 = (un)substituted (hetero)arylene; R5 = (un)substituted (hetero)aryl; n = 1-4; X = O, S; Y = (CH2)pOq (p = 1-3 and q = 0; p = 2-3 and q = 1); Z = O, a bond] which are inhibitors of the enzyme Lp-PLA2 useful in treating atherosclerosis, were prepd. Thus, reacting N-[2-(diethylamino)ethyl]-4-(4-trifluoromethylphenyl)benzylamine with 1-(carboxymethyl)-2-(4-fluorobenzylthio)-5-ethylpyrimidin-4-one in the presence of HATU and (iso-Pr)2NEt in CH2Cl2 afforded the pyrimidinone II. The compds. I described in Examples were tested for Lp-PLA2 inhibition and showed IC50 values in the range <0.1 nM to 10 .mu.M.

IT **356057-98-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrimidine-4-one derivs. as LDL-PLA2 inhibitors)

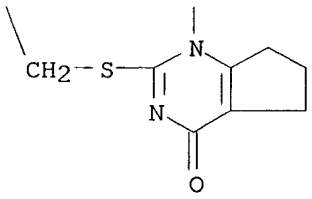
RN 356057-98-2 HCAPLUS

CN 1H-Cyclopentapyrimidine-1-acetamide, N-(1-ethyl-4-piperidinyl)-2-[[(4-fluorophenyl)methyl]thio]-4,5,6,7-tetrahydro-4-oxo-N-[[4'-(trifluoromethyl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



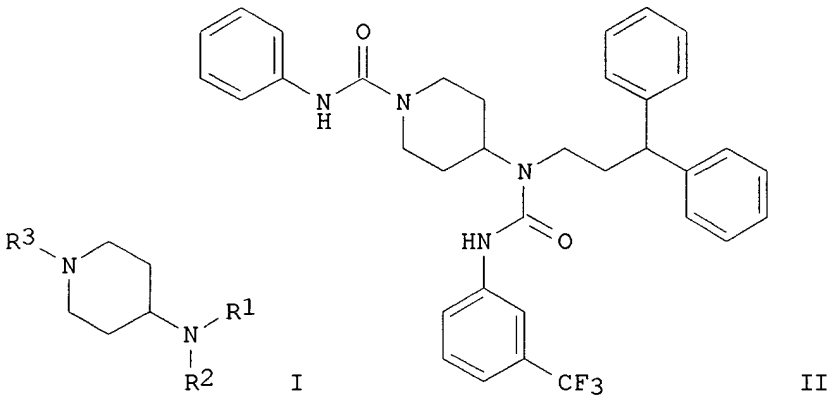
RE.CNT 4
RE
(1) Boyd; HCAPLUS
(2) Boyd; BIOORG MED CHEM LETT 2000, V10(22), P2557 HCAPLUS
(3) Fenwick, A; WO 0066567 A 2000 HCAPLUS
(4) Smith, S; WO 9924420 A 1999 HCAPLUS

L17 ANSWER 4 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:453019 HCAPLUS
DN 135:46106
TI 4-Aminopiperidine derivatives, processes for their preparation, pharmaceutical compositions, and their use as medicines, specifically as somatostatin receptor ligands
IN Thurieau, Christophe; Gonzalez, Jerome; Moinet, Christophe
PA Societe de Conseils de Recherches et d'Applications Scientifiques (S.C.R.A.S.), Fr.
SO PCT Int. Appl., 193 pp.

CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001044191	A1	20010621	WO 2000-FR3497	20001213
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2802206	A1	20010615	FR 1999-15724	19991214
PRAI	FR 1999-15724	A	19991214		

OS MARPAT 135:46106
GI



I II

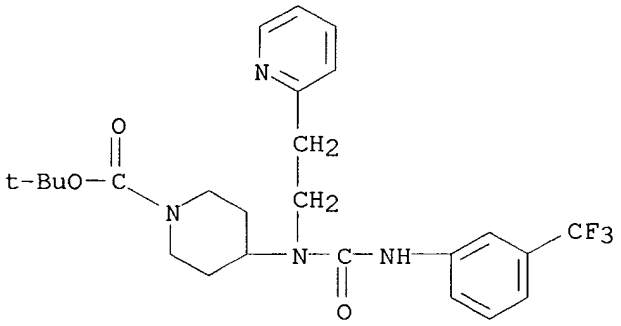
AB The invention concerns novel 4-aminopiperidine derivs. I [R1 = alkyl, alkenyl, alkynyl, (CH2)mYZ1, (CH2)mZ2, 1-benzylpiperidin-4-yl, 2-naphthylcarbamoyl, 4-benzylpiperazin-1-yl, 2-acetamidoethyl; Z1 = alkyl or (un)substituted aryl; Z2 = cyano, cyclohexenyl, bis-Ph, cycloalkyl, (un)substituted heterocycloalkyl, aryl, heteroaryl, etc.; R2 = C(Y)NHX1, C(O)X2, SO2X3; R3 = H, (un)substituted alkyl, alkenyl, alkynyl, aralkyl, C(Y)NHX1, (CH2)nC(O)X2, SO2X3, etc.; X1 = alkyl, alkenyl, alkynyl, aryl, aralkyl, etc.; X2 = wide variety of groups; X3 = alkyl, alkenyl, phenylalkenyl, CF3, (un)substituted (hetero)aryl or -aralkyl; Y = O, S; n = 0-4; m = 1-6]. Also disclosed are methods for their prepn. by parallel synthesis processes in liq. and solid phase. I have good affinity for certain sub-types of somatostatin receptors, and are particularly useful for treating pathol. conditions or diseases wherein one more somatostatin receptor sub-types are involved. Claims specifically mention acromegaly, pituitary adenoma, or endocrine gastroenteropanceatic tumors in carcinoid syndrome. A table of 778 compds. I is given, and several syntheses are

described in detail. For instance, N-BOC-4-piperidone underwent reductive amination with 3,3-diphenylpropylamine and NaBH(OAc)3, followed by reaction with 3-trifluoromethylphenyl isocyanate, removal of the BOC group with CF3CO2H, and reaction with Ph isocyanate, to give title compd. II. Some compds. I had sub-micromolar Ki for at least one of five tested somatostatin receptor subtypes (no data).

IT **344783-76-2P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of aminopiperidine derivs. as somatostatin receptor ligands)

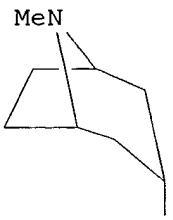
RN 344783-76-2 HCAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[2-(2-pyridinyl)ethyl][[[3-(trifluoromethyl)phenyl]amino]carbonyl]amino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

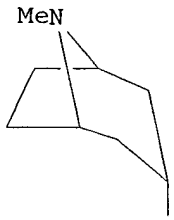


RE.CNT 4
RE
(1) Anphar Sa; DE 2751138 A 1978 HCAPLUS
(2) Pasternak, A; WO 9844921 A 1998 HCAPLUS
(3) Pasternak, A; WO 9922735 A 1999 HCAPLUS
(4) Pfizer; DE 2530894 A 1976 HCAPLUS

L17 ANSWER 5 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2001:155171 HCAPLUS
DN 134:340584
TI Parallel modification of tropane alkaloids
AU Aberle, N. S.; Ganesan, A.; Lambert, J. N.; Saubern, S.; Smith, R.
CS School of Chemistry, The University of Melbourne, Parkville, 3010, Australia
SO Tetrahedron Lett. (2001), 42(10), 1975-1977
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
GI



I



II

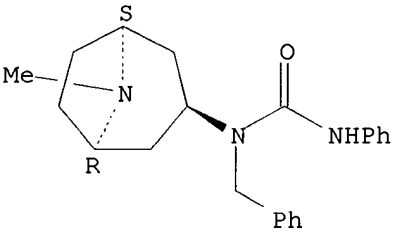
AB Various tropane alkaloids have been prepd. by structural modification of the readily available natural product, scopolamine. Reaction of isocyanates with 6,7-dehydrotropine provided a no. of urethanes, e.g. I. Reductive amination of tropinone and subsequent reaction with isocyanates provided ureas, e.g. II. Mitsunobu inversion of the C-3 alc. of tropine afforded the epimeric ester III.

IT **338389-02-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(parallel modification of tropane alkaloids)

RN 338389-02-9 HCAPLUS

CN Urea, N-[(3-endo)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-N'-phenyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 10

RE

(1) Abdel-Magid, A; J Org Chem 1996, V61, P3849 HCAPLUS
(2) Booth, R; J Am Chem Soc 1997, V119, P4882 HCAPLUS
(3) Bremner, J; Tetrahedron Lett 1996, V37, P97 HCAPLUS
(4) Dodge, J; Recent Res Dev Org Chem 1997, V1, P273 HCAPLUS
(5) Kiankarimi, M; Tetrahedron Lett 1999, V40, P4497 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 6 OF 29 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:115088 HCAPLUS

DN 134:178141

TI Preparation of oxoazacycloalkanes and analogs

IN Hulme, Christopher; Morton, George C.; Salvino, Joseph M.; Labaudiniere, Richard F.; Mason, Helen J.; Morrissette, Mathew M.; Ma, Liang; Cherrier, Marie-Pierre

PA Aventis Pharmaceutical Products Inc., USA

SO PCT Int. Appl., 176 pp.
CODEN: PIXXD2

DT Patent

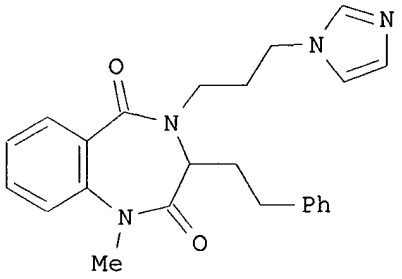
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001010799	A1	20010215	WO 2000-US21257	20000803

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-368213 A 19990804
OS CASREACT 134:178141; MARPAT 134:178141
GI

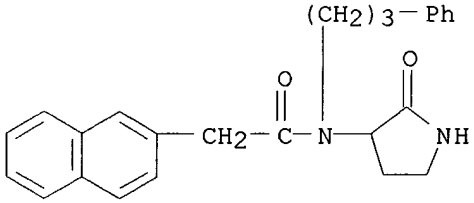


I

AB The title process comprises, e.g., Ugi condensation of N-protected anthranilic acids, amines, aldehydes, and an isocyanide followed by deprotection and cyclization. Thus, 2-(BocMeN)C6H4CO2H, imidazole-1-propanamine, PhCH2CH2CHO, and an isocyanide were combined to give title compd. I.

IT **234781-50-1P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of oxoazacycloalkanes and analogs)

RN 234781-50-1 HCAPLUS
CN 2-Naphthaleneacetamide, N-(2-oxo-3-pyrrolidinyl)-N-(3-phenylpropyl)- (9CI) (CA INDEX NAME)



RE.CNT 6
RE

(1) Bock, H; DE 19731893 A 1999 HCAPLUS
(2) Cherrier, M; WO 9938844 A 1999 HCAPLUS
(3) Hulme, C; TETRAHEDRON LETTERS 1998, V39(10), P1113 HCAPLUS
(4) Hulme, C; TETRAHEDRON LETTERS 1998, V39(40), P7227 HCAPLUS
(5) Hulme, C; TETRAHEDRON LETTERS 1998, V39(44), P8047 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

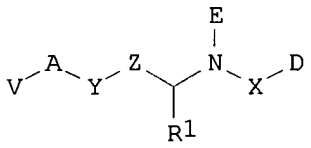
L17 ANSWER 7 OF 29 HCAPLUS COPYRIGHT 2002 ACS
AN 2000:824211 HCAPLUS
DN 134:4764
TI Preparation of 3-(benzoylamino)propionic acid derivatives as glucagon antagonists/inverse agonists
IN Ling, Anthony; Plewe, Michael Bruno; Truesdale, Larry Kenneth; Lau, Jesper; Madsen, Peter; Sams, Christian; Behrens, Carsten; Vagner, Josef; Christensen, Inge Thoger; Lundt, Behrend Frederik; Sidelmann, Ulla Grove; Thogersen, Henning
PA Novo Nordisk A/S, Den.; Agouron Pharmaceuticals, Inc.
SO PCT Int. Appl., 564 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000069810	A1	20001123	WO 2000-DK264	20000516

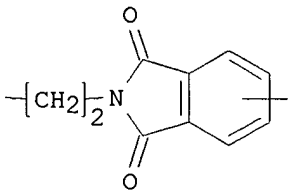
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI	DK 1999-684	A	19990517
	DK 2000-478	A	20000321

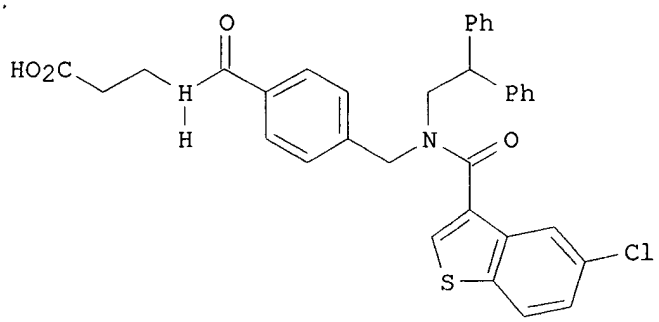
OS MARPAT 134:4764
GI



I



II



III

AB The title compds. [I; V = CO2R2, CONR2R3, CONR2OR3, etc. (wherein R2, R3 = H, alkyl); A = (CH2)n(CR8R9)bNR7, (CR8R9)b(CH2)nNR7, (CR8R9)b(CH2)n, etc. (b = 0-1; n = 0-3; R7 = H, alkyl, (cycloalkyl)alkyl; R8, R9 = H, alkyl); Y = CO, SO2, O, a bond; Z = (un)substituted phenylene, divalent radical derived from 5-6 membered heteroarom. ring contg. 1-2 heteroatoms selected from N, O and S; or AYZ together = II; R1 = H, alkyl; X = CO(CR13R14)r(CH2)s, SO2(CR13R14)r(CH2)s, CO2(CR13R14)r(CH2)s, etc. (r = 0-1; s = 0-3; R13, R14 = H, alkyl); D = (un)substituted Ph, pyridyl, cyclopropyl, etc.; E = (un)substituted quinolinyl, 2,5-dioxopiperidinyl, biphenylalkyl, etc.] which act to antagonize the action of the glucagon hormone on the glucagon receptor (data given), and therefore may be suitable for the treatment and/or prevention of any glucagon-mediated conditions and diseases such as hyperglycemia, Type 1 diabetes, Type 2 diabetes and obesity, were prepd. and formulated. E.g., a multi-step solid phase synthesis of III was given. Compds. I are effective at 0.05-10 mg/kg/day.

IT **307986-33-0P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-(benzoylamino)propionic acid derivs. as glucagon antagonists/inverse agonists)

RN 307986-33-0 HCAPLUS

CN .beta.-Alanine, N-[4-[[[1-(cyclopropylcarbonyl)-4-piperidinyl][[[4-(trifluoromethoxy)phenyl]amino]carbonyl]amino]methyl]benzoyl]- (9CI) (CA INDEX NAME)